novocaine, .beta.-eucaine, larocaine, and tutocaine decreased muscular performance. In certain doses, local anesthetics in general, including psicaine-neu, pantocaine, and percaine, stimulated the muscle. The local anesthetics antagonized I. Ascorbic acid and nicotinamide had no effect on muscle performance. NaSCN increased the muscle's power. 63 references.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:44:40 ON 07 MAY 2001)

L28 126 S L26
L29 105 S L28 NOT (L8 OR L14)
L30 48 DUP REM L29 (57 DUPLICATES REMOVED)

L34 28 S L30 AND ADMIN?

L34 ANSWER 1 OF 28 MEDLINE
ACCESSION NUMBER: 2001096059 MEDLINE
DOCUMENT NUMBER: 21033508 PubMed ID: 11185966
TITLE: A descriptive study of an epidemic of poisoning caused by heroin adulterated with scopolamine.
AUTHOR: Hamilton R J; Perrone J; Hoffman R; Henretig F M; Karkevandian E H; Marcus S; Shih R D; Blok B; Nordenholz K
CORPORATE SOURCE: New York University School of Medicine, New York City Poison Center, New York, USA..
richard.hamilton@drexel.edu
SOURCE: JOURNAL OF TOXICOLOGY. CLINICAL TOXICOLOGY, (2000) 38 (6) 597-608.
Journal code: KAN. ISSN: 0731-3810.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010117
Entered Medline: 20010201

AB OBJECTIVE: Adulterants, contaminants, and diluents are all examples of additives to street drugs. Some of these additives may be pharmacologically active; however, it is unusual for them to cause toxic side effects. In the spring of 1995, a new form of heroin appeared in New York City, spreading to other East Coast cities, that was adulterated with **scopolamine**. It caused severe anticholinergic toxicity in heroin users with patients often presenting to emergency departments in great numbers. This is a report of the demographics and clinical characteristics of the epidemic. METHODS: A combination of prospective and retrospective

data collection from the New York City, New Jersey, Delaware Valley, and Maryland Poison Centers. The primary measurements were age, sex, route of drug use, vital signs, signs and symptoms, disposition, and treatment. RESULTS: Of the 370 cases reported to the participating poison centers, 129 were excluded from the final analysis because of insufficient data. Of the patients who used this product, 55% presented with signs and symptoms of heroin toxicity but then became severely agitated with anticholinergic symptoms when naloxone was used to reverse respiratory depression. **Nasal** insufflation was the route of **administration** in 34% of the cases. Seizures were rare (3%). Ninety percent required admission, and half were admitted to a critical care unit. CONCLUSIONS: Adulteration of street drugs can lead to toxic epidemics. Poison centers are essential for identification of these trends and are the primary source of information on diagnosis and treatment.

L34 ANSWER 2 OF 28 MEDLINE
ACCESSION NUMBER: 2000099312 MEDLINE
DOCUMENT NUMBER: 20099312 PubMed ID: 10633495
TITLE: Intravenous scopolamine is potently self-**administered** in drug-naive mice.
AUTHOR: Rasmussen T; Fink-Jensen A
CORPORATE SOURCE: Health Care Discovery, Novo Nordisk A/S, Malov, Denmark.
SOURCE: NEUROPSYCHOPHARMACOLOGY, (2000 Jan) 22 (1) 97-9. Journal code: ADQ; 8904907. ISSN: 0893-133X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209
Entered Medline: 20000128

AB **Scopolamine** self-**administration** was investigated in an acute model using drug-naive mice. The mice could self-**administer** intravenous infusions contingent on **nose** poking and were tested in pairs using a contingent and a yoked control mouse. Upon **nose** poking of the contingent mouse, both mice received an intravenous infusion of either saline or **scopolamine** (fixed ratio 1). An inverted U-shaped unit dose-response curve was seen with the contingent mice. The unit dose at which **nose** poking of the contingent mice peaked (mean 375 per 30 min) was 0.1 mg/kg/infusion. **Nose** poking of yoked control mice also increased dose dependently, but it was significantly lower than that of the contingent mice. The apparent **scopolamine**-induced dose-dependent hyperactivity was, however, unlikely in itself to form the entire basis for the

increase in **nose** poking of the contingent mice. The results demonstrate that **scopolamine** has acute and reinforcing properties in drug naive mice.

L34 ANSWER 3 OF 28 MEDLINE
ACCESSION NUMBER: 1999050134 MEDLINE
DOCUMENT NUMBER: 99050134 PubMed ID: 9832940
TITLE: An automated learning and memory model in mice: pharmacological and behavioral evaluation of an autoshaped response.
AUTHOR: Vanover K E; Barrett J E
CORPORATE SOURCE: Central Nervous System Research Department, Lederle Laboratories, American Cyanamid Co., Pearl River, New York, USA.
SOURCE: BEHAVIOURAL PHARMACOLOGY, (1998 May) 9 (3) 273-83. Journal code: CM8; 9013016. ISSN: 0955-8810.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981229

AB The purpose of the present experiments was to develop and validate pharmacologically an automated, relatively rapid, and reproducible behavioral model of learning and memory using an autoshaping procedure in mice. **Nose**-poke responses into a recessed area were differentiated by response-dependent reinforcement during two identical consecutive daily sessions. Performance during the first session was considered to be a measure of acquisition and that during the second session a measure of retention. Sensitivity to procedural manipulation, as well as an index of learning under these conditions, was demonstrated, for example, by a decrease in response rate when **nose**-poke responses did not produce a reinforcer. The sensitivity of the paradigm to pharmacological intervention was examined after drug **administration** before the first session. **Scopolamine** (0.1-10.0 mg/kg) had no effect on acquisition but caused a significant dose-related impairment of retention. Dizocilpine (0.01-1.0 mg/kg) impaired both acquisition and retention performance. 8-Hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT; 0.1-1.0 mg/kg) disrupted behavior in general, but failed to have a selective effect on acquisition or retention. Linopirdine (0.1-1.0 mg/kg) showed only a weak enhancement of acquisition, whereas 4-aminopyridine (4-AP; 0.1-1.0 mg/kg) significantly facilitated acquisition. This paradigm offers the potential for a rapid, objective, and reliable indication of whether a drug will affect the acquisition or retention of a

positively reinforced response in mice and could be a useful supplement to existing procedures.

L34 ANSWER 4 OF 28 MEDLINE
ACCESSION NUMBER: 97016661 MEDLINE
DOCUMENT NUMBER: 97016661 PubMed ID: 8863287
TITLE: Bioavailability of **intranasal** **scopolamine** in normal subjects.
AUTHOR: Putcha L; Tietze K J; Bourne D W; Parise C M; Hunter R P; Cintron N M
CORPORATE SOURCE: Biomedical Operations and Research Branch, NASA-Johnson Space Center, Houston, TX 77058, USA.
SOURCE: JOURNAL OF PHARMACEUTICAL SCIENCES, (1996 Aug) 85 (8) 899-902.
Journal code: JO7; 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19970219
Last Updated on STN: 19970219
Entered Medline: 19970130

AB The bioavailability of **scopolamine** in three dosage forms was compared in 12 healthy nonsmoking male volunteers. Subjects received 0.4-mg doses of **scopolamine** bromide in intravenous (i.v.), **intranasal** (i.n.), or oral (p.o.) dosage forms on three occasions, with at least 2 weeks separating the doses. **Scopolamine** concentrations in plasma were determined with a combined reverse-phase liquid chromatographic-radioreceptor binding assay. Saliva volume and flow rate and percent suppression of control flow rate were determined from each sample. Absorption after i.n. and po **scopolamine** **administration** was rapid; plasma concentrations [1680 (i.n.) and 164 pg/mL (p.o.)] peaked within 1 h of dosing [0.37 (i.n.) and 0.78 h (p.o.)], respectively. i.n. and i.v. **scopolamine** suppressed salivary flow rate to similar extents (95% and 99.7%), respectively. Times to reach maximum effect were 1.05 and 0.27 h after i.n. and i.v. dosage, respectively. Absolute **intranasal** bioavailability, calculated from the area under the drug concentration vs time curve, was found to be significantly greater than that of p.o. **scopolamine** (83% vs 3.7%, $p < 0.05$). The i.n. route may provide a noninvasive, reliable, fast, and effective route for **administering** **scopolamine**.

L34 ANSWER 5 OF 28 MEDLINE
ACCESSION NUMBER: 96108594 MEDLINE
DOCUMENT NUMBER: 96108594 PubMed ID: 8531068

TITLE: Effects of chronic haloperidol on reaction time and errors in a sustained attention task: partial reversal by anticholinergics and by amphetamine.

AUTHOR: Brockel B J; Fowler S C
CORPORATE SOURCE: Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, New York, USA.

CONTRACT NUMBER: MH43429 (NIMH)
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1995 Dec) 275 (3) 1090-8.
Journal code: JP3; 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960220
Last Updated on STN: 19960220
Entered Medline: 19960201

AB The attentional and motor-disruptive effects of low doses of haloperidol were studied in a sustained attention task performed by rats. Five separate groups (n = 7 or 8) of rats were trained to react to a 0.125-sec visual stimulus by executing a **nose** -poke response within 3 sec of stimulus presentation. Each group of rats received its own dose (0.0, 0.02, 0.04, 0.08 or 0.12 mg/kg) of haloperidol daily for 3 months, and from the 1st week onward dose-effects on reaction time were quite stable across time. Haloperidol treatment disrupted the sustained attention task performance by decreasing the number of behavior-initiated stimulus presentations, decreasing the number of reinforcers earned, increasing the proportion of errors of omission and increasing reaction time to the target stimulus. Testing of challenge drugs began after 23 days of haloperidol treatment. **Scopolamine** (0.1 and 0.2 mg/kg), benztropine (1.0, 3.0 and 6.0 mg/kg) and d-amphetamine (0.25, 0.5, 1.0 and 2.0 mg/kg) ameliorated haloperidol-induced reaction time slowing, whereas only benztropine and amphetamine lessened haloperidol-induced errors of omission. The 2.0-mg/kg dose of amphetamine by itself produced a significant increase in errors of omission without affecting reaction time. Haloperidol effectively normalized this amphetamine-induced disruption in attention. The results are consistent with a dopaminergic involvement in the expression of both attention and motor processes.

L34 ANSWER 6 OF 28 MEDLINE
ACCESSION NUMBER: 95127094 MEDLINE
DOCUMENT NUMBER: 95127094 PubMed ID: 7826513
TITLE: Working memory tasks in five-choice operant chambers:

use of relative and absolute spatial memories.

AUTHOR: Gutnikov S A; Barnes J C; Rawlins J N
CORPORATE SOURCE: Department of Experimental Psychology, University of Oxford, England.

SOURCE: BEHAVIORAL NEUROSCIENCE, (1994 Oct) 108 (5) 899-910.
Journal code: AG4; 8302411. ISSN: 0735-7044.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950307
Last Updated on STN: 19950307
Entered Medline: 19950223

AB Rats were trained to **nose** poke into illuminated holes to perform 1 of 2 different spatial working memory tasks (relative recency or reward history) in a 5-choice operant chamber. A series of experiments indicated that choice accuracy on both tasks depended on (a) the holes' spatial separation, and (b) their relative rather than absolute positions. The results suggest that accurate choice depended on using a motor mediation strategy to turn, so as to encounter the target (correct) hole before encountering the alternative (wrong) hole. The drugs **administered** to the rats, d-amphetamine, **scopolamine**, and CGP-37849 impaired choice accuracy on these tasks, even though task performance had not appeared to depend on explicit memory for the sample responses. This suggests that parallel drug effects obtained on other operant matching- or nonmatching-to-position tasks may not have reflected truly amnesic effects of the drug treatments.

L34 ANSWER 7 OF 28 MEDLINE

ACCESSION NUMBER: 93066661 MEDLINE
DOCUMENT NUMBER: 93066661 PubMed ID: 1438507

TITLE: Scopolamine increases nonreinforced behavior in an intracranial self-stimulation discrimination paradigm.

AUTHOR: Agars K; Kokkinidis L
CORPORATE SOURCE: Department of Psychology, University of Saskatchewan, Saskatoon, Canada.

SOURCE: PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR, (1992 Oct) 43 (2) 657-60.
Journal code: P3Q; 0367050. ISSN: 0091-3057.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199212
ENTRY DATE: Entered STN: 19930122

Last Updated on STN: 19930122
Entered Medline: 19921222

AB The effects of several doses of systemic **scopolamine** **administration** on brain-stimulation reward from the A10 nucleus of the ventral tegmental area (VTA) were evaluated. The intracranial self-stimulation (ICSS) task involved a two-hole **nose**-poke procedure allowing for the assessment of both reinforced (correct) and nonreinforced (incorrect) performance levels as a function of varying current intensities. **Scopolamine** (0.75, 1.5, and 3.0 mg/kg) was found not to alter the rate-intensity functions derived from descending and ascending presentation of seven current levels. However, when nonreinforced behavior was considered significant increases in error responding were evident following **scopolamine** injection. These results are consistent with the known disinhibitory and perseverative properties of **scopolamine**, and indicate that the previously reported positive actions of peripheral **administration** of anticholinergic drugs on ICSS likely involved a drug-induced rate-enhancement of reward-unrelated performance variables.

L34 ANSWER 8 OF 28 MEDLINE
ACCESSION NUMBER: 93008417 MEDLINE
DOCUMENT NUMBER: 93008417 PubMed ID: 1394571
TITLE: [Multiple (serial) poisoning with **scopolamine** present in a compounded **nose** drop preparation].
Vicecetna (seriova) intoxikace skopolaminem obsazenym v magistraliter pripravenych nosnich kapkach.
AUTHOR: Marx D; Janeckova M; Kminek A
CORPORATE SOURCE: Klinika deti a dorostu 3. LF UK a FN Kralovske Vinohrady, Praha.
SOURCE: CESKOSLOVENSKA PEDIATRIE, (1992 Sep) 47 (9) 553-5.
Journal code: CW3; 0403576. ISSN: 0069-2328.
PUB. COUNTRY: Czechoslovakia
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Czech
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921125

AB The authors describe three cases of **scopolamine** intoxication which was added to **nasal** drops instead of Mucoseptonex. An account is given of the characteristics of **scopolamine** intoxication and of possible therapy.

L34 ANSWER 9 OF 28 MEDLINE

ACCESSION NUMBER: 92354971 MEDLINE
DOCUMENT NUMBER: 92354971 PubMed ID: 1644341
TITLE: Does nasal oxygen reduce the cardiorespiratory problems experienced by elderly patients undergoing endoscopic retrograde cholangiopancreatography?..
COMMENT: Comment in: Gut. 1993 Feb;34(2):288
AUTHOR: Haines D J; Bibbey D; Green J R
CORPORATE SOURCE: Gastroenterology Department, North Staffs Hospital Centre, Stoke-on-Trent.
SOURCE: GUT, (1992 Jul) 33 (7) 973-5.
Journal code: FVT; 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199209
ENTRY DATE: Entered STN: 19920925
Last Updated on STN: 19920925
Entered Medline: 19920908

AB Elderly patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) have an increased risk of sedation related complications during the procedure. To determine whether **nasal** oxygen supplementation (2 l/min) reduces these risks, half of 66 patients aged over 60 undergoing ERCP using minimal midazolam sedation alone were randomised to receive **nasal** oxygen. The arterial oxygen saturation and pulse rate of all patients were monitored by pulse oximetry before and during the procedure. Only three patients in the oxygen supplemented group (n = 33) required any form of intervention for hypoxia compared with six in the control group (n = 33). Comparison of mean arterial oxygen saturation between the groups showed significantly higher levels in the **nasal** oxygen group throughout the procedure. Pulse rate comparisons showed no significant difference from control group values, both groups had short periods of significant tachycardia. We conclude that minimal sedation with midazolam alone still produces hypoxia during ERCP in a substantial number of elderly patients. **Nasal** oxygen supplementation increases the level of patient oxygenation and reduces the need for intervention, but does not reduce tachycardia in the elderly patient. Because **hyoscine** may be a significant factor contributing to the tachycardia, sparing rather than routine use of this agent is advisable.

L34 ANSWER 10 OF 28 MEDLINE
ACCESSION NUMBER: 91147833 MEDLINE
DOCUMENT NUMBER: 91147833 PubMed ID: 2290070
TITLE: Review: systemic absorption of topically applied

ocular drugs in humans.
AUTHOR: Salminen L
CORPORATE SOURCE: Department of Ophthalmology, Tampere University Central Hospital, Finland.
SOURCE: JOURNAL OF OCULAR PHARMACOLOGY, (1990 Fall) 6 (3) 243-9. Ref: 28
Journal code: IRG; 8511297. ISSN: 8756-3320.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199104
ENTRY DATE: Entered STN: 19910419
Last Updated on STN: 19910419
Entered Medline: 19910403

AB Literature on human plasma concentrations after instillation of ocular timolol, levobunolol, atropine, cyclopentolate, **scopolamine**, phenylephrine, betamethasone and technetium Tc 99m and theories of lacrimal drainage were reviewed. In all studies the eyedrops absorbed rapidly into the systemic circulation. Like the kinetics of the tracer substances in lacrimal scintigraphy, the plasma drug levels showed interindividual variations. Plasma levels of ocular drugs were lower when punctal occlusion was applied, the mechanism, however, could not be explained. Since an early and a late plasma peak was occasionally registered in some subjects in timolol and cyclopentolate studies, it is suggested that systemic absorption of ocular drugs is low during the nasolacrimal passage but occurs during conjunctival and **nasal** contact.

L34 ANSWER 11 OF 28 MEDLINE
ACCESSION NUMBER: 88332943 MEDLINE
DOCUMENT NUMBER: 88332943 PubMed ID: 3047394
TITLE: Transdermal scopolamine in drooling.
AUTHOR: Brodtkorb E; Wyzocka-Bakowska M M; Lillevold P E; Sandvik L; Saunte C; Hestnes A
CORPORATE SOURCE: Department of Neurology, Trondheim University Hospital, Norway.
SOURCE: JOURNAL OF MENTAL DEFICIENCY RESEARCH, (1988 Jun) 32 (Pt 3) 233-7.
Journal code: J4N; 0375401. ISSN: 0022-264X.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198810
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881020

AB The effect of oral anticholinergic drugs has been limited in the treatment of drooling. Transdermal **scopolamine** (1.5 mg/2.5 cm2) offers advantages. One single application is considered to render a stable serum concentration for 3 days. A distinct reduction of basal salivation was demonstrated in an open trial of six healthy volunteers. Eighteen mentally retarded patients with a drooling problem were studied in a double-blind, placebo-controlled cross-over trial. The therapeutic effect of transdermal **scopolamine** was assessed by a visual analogue scale. Three patients dropped out due to loss of the system. In the remaining 15 patients, the active drug caused a reduction of drooling which was significant in the period from 24 to 72 h. There were few and slight objective signs of unwanted effects. Scopoderm may cause drowsiness and affect tooth health. The management of drooling should primarily be focused on the cause. Sensomotor training is often valuable in cerebral palsy. Factors such as **nasal** obstruction, mucosal irritation, and drug-induced parkinsonism should be given attention. Sometimes, however, a temporary symptomatic treatment is indicated, for example on special occasions or in order to cure peri-oral skin lesions. Transdermal **scopolamine** may offer this possibility.

L34 ANSWER 12 OF 28 MEDLINE
ACCESSION NUMBER: 86192688 MEDLINE
DOCUMENT NUMBER: 86192688 PubMed ID: 3699092
TITLE: Motor effects of calcitonin **administered** intracerebroventricularly in the rat.
AUTHOR: Twery M J; Kirkpatrick B; Critcher E C; Lewis M H; Mailman R B; Cooper C W
CONTRACT NUMBER: AM-17743 (NIADDK)
AM-32060 (NIADDK)
HD-03110 (NICHD)
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1986 Feb 18) 121 (2) 189-98.
Journal code: EN6; 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198605
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860528

AB In rats treated with salmon calcitonin (CT) **administered**

intracerebroventricularly (i.c.v., 85 or 8.5 pmol), spasmodic body movements, hopping and tail jerks, collectively termed dyskinesia, appeared within 1 h of **administration** and persisted for at least 24 h. In addition, spontaneous grooming, rearing and locomotion occurred less often in CT-treated rats than in vehicle-injected animals, while the incidence of both sniffing and **nose** poking remained essentially unchanged. The CT failed to displace either [3H]dopamine or [3H]spiperone from striatal membranes, and the behavioral effects were not blocked by haloperidol or SCH 23390, suggesting that the peptide did not directly affect dopamine receptors. The dyskinesia was not blocked by **scopolamine**, atropine, muscimol, diazepam or ketanserin. These data are consistent with the hypothesis that a compound with recognition characteristics similar to those of salmon CT may function as a neurotransmitter-modulator in the central nervous system.

L34 ANSWER 13 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:120261 BIOSIS
DOCUMENT NUMBER: PREV200100120261
TITLE: Rapid assessment of operant learning and memory in mice.
AUTHOR(S): Hain, H. S. (1); Baron, S. P.; Meltzer, L. T.
CORPORATE SOURCE: (1) Parke-Davis Pharmaceutical Research Division, Ann Arbor, MI USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-840.23. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Previous studies in our lab have shown that mice can rapidly acquire an operant learning task (Baron and Meltzer, Soc. Neurosci. Abst. 1999). The objective of the present experiments was to optimize this response acquisition task. Male C57BL/6J mice were utilized in a three-day procedure. Day 1 of training (dipper training) mice were acclimated for one hour to the operant test chamber and dipper presentation of evaporated milk on a variable-time 60 sec schedule. On day 2 (response acquisition) mice were placed in operant chambers with two illuminated **nose**-poke holes. A **nose** poke in one hole resulted in an audible click and 10-sec presentation of evaporated milk, while **nose** pokes in the other hole resulted only in an audible click. Sessions ended after 20 dipper presentations or 30 min. On day 3 (retention) the response consequences were the same for the **nose**-poke holes, but

sessions ended after an hour with no response limit. On the response acquisition day, 19 of the 24 mice obtained all 20 dipper presentations. These 19 mice demonstrated learning on the retention testing when compared to acquisition day performance. This was measured by a reduction in latency to obtain 20 dipper presentations and a decrease of **nose** pokes in the inoperative hole as compared to total **nose**-poke responses. In separate groups of mice, **scopolamine** (1 and 3.2 mg/kg, i.p.) **administered** prior to the response acquisition did not alter the number of mice obtaining 20 dipper presentations as compared to no-treatment and saline groups. Retention, however, was disrupted in mice previously injected with **scopolamine**. This was measured by a difference between the drug-induced groups and saline/no-treatment groups in latency to obtain 20 dipper presentations and inoperative **nose**-pokes as compared to total **nose**-poke responses.

L34 ANSWER 14 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:228234 BIOSIS
DOCUMENT NUMBER: PREV199698784363
TITLE: 2,4-Dithiobiuret in rats: Cognitive facilitation after acute injection precedes motor impairment after repeated daily injections.
AUTHOR(S): Bushnell, Philip J. (1); Oshiro, Wendy M.
CORPORATE SOURCE: (1) Neurotoxicology Division, US Environmental Protection Agency, Research Triangle Park, NC USA
SOURCE: Psychopharmacology, (1996) Vol. 123, No. 3, pp. 267-279.
ISSN: 0033-3158.
DOCUMENT TYPE: Article
LANGUAGE: English

AB 2,4-Dithiobiuret (DTB) is a sulfonated derivative of urea that is used as a reducing agent in chemical manufacture. Its low acute toxicity to rodents belies a peripherally mediated, delayed-onset muscle weakness which develops during repeated daily exposure. In experiment 1, a standard dose regimen of DTB (0.5 mg/kg per day IP for 5 days) was used to induce motor dysfunction as a way to dissociate peripheral and central influences on a test of cognitive and motor function in rats. Sixteen male rats were trained to perform a Delayed Matching-to-Position/Visual Discrimination (DMTPND) task which permits quantification of working memory (matching accuracy), reference memory (discrimination accuracy), and motor function (choice response latency and **nose**-poke inter-response time, IRT). The first dose of DTB significantly increased matching accuracy; during the following week, DTB reduced matching accuracy, increased choice response latency and nosepoke IRT, and reduced trial completion. Discrimination accuracy remained unaffected. Experiment 2 explored the effects of single

administrations of DTB on DMTP/VD. Sixteen other trained rats were divided into two groups with equal matching accuracy. One group received DTB (0.5, 1.0, and 2.0 mg/kg, IP) in separate injections at least 1 week apart; the other group received vehicle at the same times. Matching accuracy increased significantly in the treated rats and not in the controls following each dose of DTB. The magnitude of this increase was dose-dependent, and lasted from 1 to 8 weeks after each injection. Discrimination accuracy, response latency, nosepoke IRT and trial completion remained unaffected throughout the study. After DTB, matching accuracy was less easily disrupted by **scopolamine** (0.1-0.3 mg/kg, IP). However, DTB did not alter the rats' response to reducing the distance between the response levers, to reversal of the matching rule to a nonmatching rule, or to challenge with MK-801 (0.05-0.10 mg/kg, IP). These data indicate that acute DTB causes a long-lasting facilitation of working memory in rats in the absence of any of the indications of motor impairment which follow repeated, daily injections of the chemical.

L34 ANSWER 15 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1982:283706 BIOSIS
DOCUMENT NUMBER: BA74:56186
TITLE: COMPARISON OF OLD AND NEW TYPES OF PRE MEDICATIONS.
AUTHOR(S): KANTO J; PAKKANEN A; KANGAS L; LEPPANEN T
CORPORATE SOURCE: DEP. ANAESTHESIOL., TURKU UNIV. CENTRAL HOSP., SF-20520 TURKU 52.
SOURCE: INT J CLIN PHARMACOL THER TOXICOL, (1982) 20 (4), 187-189.
CODEN: IJCPB5. ISSN: 0300-9718.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB In the treatment of transient insomnia and anxiety caused by anesthesia and surgery, the effectiveness of different benzodiazepines as oral premedicants was studied. By random allocation 41 patients received 1 mg flunitrazepam orally the night before operation and 1 mg on the morning of operation (group 1) and another 41 received 100 mg pentobarbital orally the night before operation, followed by i.m. **scopolamine** (0.006 mg/kg) + morphine (0.02 mg/kg) on the morning of operation (group 2). All patients received 0.5 mg atropine i.v. just before the induction of anesthesia. The patients in group 2 were better sedated and had less salivary secretion than those in group 1, but otherwise both were comparable. In group 2 the induction requirements of thiopentone were significantly decreased in comparison with group 1, again indicating a more potent sedative effect. Because even in the total scoring of the results there was no significant difference between the 2 groups, the easy oral route of **administration** of flunitrazepam offers a clinically relevant alternative to the

conventional premedication. In some of these [ear-**nose**-throat] patients who received flunitrazepam, i.v. atropine given just before the induction of anesthesia did not prevent salivary secretion. Oral benzodiazepine derivatives (flunitrazepam) were apparently useful before surgery as the old type old premedication (oral pentobarbital + i.m. **scopolamine** and morphine).

L34 ANSWER 16 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94012133 EMBASE
DOCUMENT NUMBER: 1994012133
TITLE: Anesthetic management in a cleft palate patient with Beckwith-Wiedemann syndrome.
AUTHOR: Kim Y.; Hirota Y.; Shibutani T.; Niwa H.; Hori T.; Akita M.; Suzuki M.; Matsuura H.
CORPORATE SOURCE: Department of Dental Anesthesiology, Faculty of Dentistry, Osaka University, 1-8 Yamadaoka,Suita, Osaka 565, Japan
SOURCE: Journal of Japanese Dental Society of Anesthesiology, (1993) 21/4 (793-799).
ISSN: 0386-5835 CODEN: NSMZDZ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; Japanese

AB Palatoplasty, partial tongue resection, and frenotomy for a one year old baby with Beckwith-Wiedemann syndrome were scheduled under general anesthesia. This syndrome was first described by Beckwith in 1963 and by Wiedemann in 1964. It is characterized by exopthalmos, macroglossia, gigantism and many other clinical features (Fig. 1-3, Table 3); it is also called EMG syndrome. Problems associated with anesthetic management in this case are hypoglycemia and macroglossia. Careful intraoperative plasma glucose monitoring is particularly important to prevent the neurologic sequelae of unrecognized hypoglycemia. It is to be expected that airway management with be complicated by the macroglossia, which may cause difficult bag/mask ventilation and endotracheal intubation following the induction of anesthesia and muscle paralysis. The patient was premedicated with 0.2 mg of **scopolamine** intramuscularly, and after 20 min, she was brought to the operating room. Following intravenous sedation with 3.75 mg of diazepam, laryngoscopy was employed for easy visualization of the glottis, and bag/mask ventilation permitted further **administration** of 30 mg of thiopental. Monitors consisted of ECG, precordial stethoscope, sphygmomanometer, and pulse oximeter. Anesthesia was induced with another 50 mg of thiopental and 1.6 mg of vecuronium. Although bag/mask ventilation was not easy, laryngoscopy and orotracheal

intubation were performed without difficulty. Anesthesia was maintained with 66% nitrous oxide in oxygen, and isoflurane (0.8% to 1.5%) under assisted ventilation. After palatoplasty, with another 1.2 mg vecuronium, a nasotracheal tube was inserted in place of the orotracheal tube for partial tongue resection and frenotomy. The intraoperative progress was uneventful. Arterial blood gases were stable (Fig. 4), and the plasma glucose and insulin level were kept within normal ranges (Table 2). Prior to extubation, we prepared a soft **nasal** airway formed from an endotracheal tube for the constriction of the pharyngeal space caused by the surgical procedures. Immediately after extubation, there was no necessity for inserting the tube in our judgement. Four hr after the end of surgery, however, slight airway obstruction was noted when she laid on her back. A nasopharyngeal airway was inserted and remained until the next morning. Since then, no remarkable changes or complications have been seen. These observations emphasize the need for cautious pre- and post-operative airway management for such difficult cases with airway problems.

L34 ANSWER 17 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93077081 EMBASE
DOCUMENT NUMBER: 1993077081
TITLE: Anesthetic management in a cleft palate patient with kabuki make-up syndrome.
AUTHOR: Sugiyama K.; Yokoyama K.; Irifune M.; Ohse K.; Ohkubo F.; Negishi M.; Mimura T.; Mietani W.
CORPORATE SOURCE: Department of Dental Anesthesia, Kagoshima University Dental Hospital, 8-35-1 Sakuragaoka,Kagoshima 890, Japan
SOURCE: Journal of Japanese Dental Society of Anesthesiology, (1993) 21/1 (101-105).
ISSN: 0386-5835 CODEN: NSMZDZ
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese

AB Palatoplasty for a two year old girl complicated with kabuki make-up syndrome was scheduled under general anesthesia. The peculiar features of this syndrome are characterized by long and slim eyes with lower palpebral eversions resembling the make-up of a kabuki actor, as first reported by Niikawa et al. and Kurokawa et al. in 1981. Multiple congenital anomalies (Fig. 1-3), mental retardation, postnatal dwarfism, and susceptibility to infection are prominent clinical findings of this syndrome with unknown etiology. The worry points for anesthesia were her severe tendency for systemic

convulsions of uncertain cause and respiratory insufficiency induced by the operation. For a successful sedation, 0.25 mg of **scopolamine** and 10 mg of pentazocine were given 45 minutes before induction; then isoflurane and nitrous oxide with 33% oxygen were used for slow induction. During anesthesia, the tidal volume was adjusted to be maintained at 40 mmHg of the PCO2 by blood gas determination (Table 2) in order to avoid respiratory alkalosis, which occasionally induces convulsions. Prior to extubation, a soft **nasal** airway was inserted via her nasopharyngeal canal and remained until the next day as a support against any constriction of the pharyngeal space by the palatoplasty. No remarkable changes or complications (Table 3) were seen throughout the perioperative period.

L34 ANSWER 18 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92049771 EMBASE
DOCUMENT NUMBER: 1992049771
TITLE: Effects of premedication with atropine or scopolamine on the pH of upper airway secretion.
AUTHOR: Cavaliere F.; Masieri S.; Schiavello R.
CORPORATE SOURCE: Istituto di Anestesiologia e Rianimazione, Universita Cattolica del S. Cuore, Largo A. Gemelli 8, 00168 Roma, Italy
SOURCE: Perspectives in E.N.T. - Immunology, (1991) 5/1 (43-48).
ISSN: 1120-2556 CODEN: PEEIE5
COUNTRY: Italy
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
015 Chest Diseases, Thoracic Surgery and Tuberculosis
024 Anesthesiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; Italian
AB The pH of **nasal** secretion was measured 'in situ' in thirty patients before premedication for surgical procedures and 15, 30, and 45 minutes later. Patients underwent three different premedications. Group A (ten patients) only received diazepam, group B (ten patients) received diazepam plus atropine, and group C (ten patients) received diazepam plus **scopolamine**. No difference was observed initially among the three groups of patients in comparison with ten healthy subjects who did not undergo any surgical procedure. Following premedication, patients who received atropine or **scopolamine** showed a significant decrease of pH; on the contrary, group A resulted unaffected. In spite of the more pronounced effect of **scopolamine** on the volume of

respiratory secretion, groups B and C showed similar trends of pH. The reduction of the pH of respiratory secretion caused by atropine and **scopolamine** may significantly contribute to the impairment of mucociliary clearance which both these drugs can cause.

L34 ANSWER 19 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 90225040 EMBASE
DOCUMENT NUMBER: 1990225040
TITLE: Ocular drugs and anesthesia.
AUTHOR: McGoldrick K.E.
CORPORATE SOURCE: Department of Anesthesiology, Yale University School of Medicine, New Haven, CT 06510, United States
SOURCE: International Anesthesiology Clinics, (1990) 28/2 (72-77).
ISSN: 0020-5907 CODEN: IACLAV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Just as anesthetic drugs sometimes affect intraocular physiology, so too can ophthalmic drugs, **administered** topically, intraocularly, or systemically, have important anesthetic implications. I will describe some of these interactions in this chapter. Systemic absorption of topical ophthalmic drugs occurs from either the conjunctiva or the **nasal** mucosa following drainage through the nasolacrimal duct. Medication tends to be absorbed slowly and minimally from the conjunctiva, which is relatively waterproof and is vastly more impervious than the thinner epithelium covering the cornea. Absorption is much more rapid and extensive from mucosal surfaces. In conscious patients, drugs are transported through the lacrimal apparatus to the **nasal** mucosa, where systemic absorption takes place-not infrequently producing undesirable systemic effects. Occluding the nasolacrimal duct by means of pressure on the inner canthus of the eye-for a few minutes after each instillation-greatly reduces absorption. Indeed, finger pressure over the duct for 5 minutes decreases systemic absorption by 67% [1], and simply keeping the eye gently closed for 5 minutes after **administering** eye drops can reduce absorption by as much as 65%. Because the lacrimal apparatus is dependent on an active blink reflex and on muscle activity, the degree of systemic absorption of eye drops is impressively reduced under general anesthesia. Nonetheless, nasolacrimal duct occlusion is recommended-even with general anesthesia-in small children who are highly susceptible to the toxic effects of certain ocular drugs,

including the belladonna alkaloids. One should also be aware that some percutaneous absorption from spillover through the immature epidermis of premature infants may occur [2]. Factors thought to predispose to adverse systemic effects following topical eye medication include overdosage (excessively concentrated solution or too many drops), especially in children; the concomitant use of adrenergic modifying drugs; the presence of a markedly inflamed or postsurgical eye in which the conjunctiva is not intact; and an elderly patient population with coronary or cerebral artery disease. Some potentially worrisome topical ocular drugs include atropine, cocaine, cyclopentolate, echothiophate iodide, epinephrine, pilocarpine, phenylephrine, **scopolamine**, timolol, and tropicamide. In addition, intraocular use of such substances as acetylcholine, epinephrine, sulfur hexafluoride, octafluorocyclobutane, and perfluoropropane may have important anesthetic implications. Last, certain ocular medications or diagnostic agents given systemically may have deleterious anesthetic implications; these agents include glycerol, mannitol, acetazolamide, methazolamide, and fluorescein.

L34 ANSWER 20 OF 28 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 79259157 EMBASE
DOCUMENT NUMBER: 1979259157
TITLE: Street drugs 1977: Changing patterns of recreational use.
AUTHOR: Siegel R.K.
CORPORATE SOURCE: Dept. Psychiat. Biobehav. Sci., Univ. California, Los Angeles, Calif., United States
SOURCE: Drug Abuse and Alcoholism Review, (1978) 1/1 (1-13).
CODEN: DAARDL
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English

AB Several summary speculations about future street drug use are possible in light of this review. Cocaine and **intranasal** drugs will increase in street use. In the future, we may speculate that cocaine will continue to be the stimulant and recreational drug of choice. Increasing user familiarity with cocaine adulterants and the **intranasal** route will further increase the experimental **intranasal** use of other compounds, particularly those with alleged stimulant properties. Herbal preparations will be more widespread and commonly accepted substitutes for controlled substances. This will proliferate through sales in mail-order houses, health food stores, and perhaps even

'legal high shops'. Indeed, a recent article in Free Enterprise (Moershell, 1977) tells prospective business people in the field 'how to profit from the drug trade without going to jail' and cites one 'lettuce opium' dealer who is making $1,500 per day on sales of extracted lettuce products. Psilocybin will become the most common street hallucinogen, other than marihuana. This trend will be realized primarily through the proliferation of sales of mushroom spores and growing kits which enable users to cultivate their own products cheaply, reliably, and discreetly. Sales of other uncontrolled hallucinogens (San Pedro cactus, morning glory seeds, etc.) will not increase significantly due to user awareness of unpleasant side effects. PCP use will escalate. Primarily due to its economic considerations, PCP will continue to be a common adulterant in street psychedelics and will become increasingly more available as a drug by itself. New exotic psychedelics will appear. These latter compounds, already detected by SDA labs, will include the substituted amphetamines (e.g., MMDA, TMA, TMA-2, DOB, etc.), jimson weed (atropine and **scopolamine**), yohimbine, and ibogaine.
Street drug users will become more informed and adverse reactions will decrease. The epidemic diffusion of drug-oriented publications and their publishing success will probably result in increased user awareness of all aspects of street drugs. To the extent that this information remains generally reliable and responsible (from a medical, not legal perspective), this should result in more informed street drug use and fewer clinical problems. The outcome of this movement has potential political significance with respect to the legal status of many street drugs. Future directions will differ only in substance, not spirit from past events.

L34 ANSWER 21 OF 28 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-072114 [09] WPIDS
CROSS REFERENCE: 2001-041263 [04]
DOC. NO. CPI: C2001-020465
TITLE: Stable, well-tolerated composition for **intranasal administration** of water-insoluble drugs e.g. **scopolamine**, comprising solution of drug in neutral oil, especially triglyceride.
DERWENT CLASS: B05
INVENTOR(S): KLOECKER, N
PATENT ASSIGNEE(S): (HEXA-N) HEXAL AG
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 19925290	A1	20001207	(200109)*		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 19925290	A1	DE 1999-19925290	19990602

PRIORITY APPLN. INFO: DE 1999-19925290 19990602
AN 2001-072114 [09] WPIDS
CR 2001-041263 [04]
AB DE 19925290 A UPAB: 20010213
NOVELTY - A pharmaceutical composition (A) for **intranasal administration** comprises a solution of at least one water-insoluble or sparingly water-soluble active agent (I) in neutral oil (II).

ACTIVITY - Anticholinergic; tranquilizer; anxiolytic; anti-addictive; analgesic; antiemetic; antiparkinson; antihistamine.

MECHANISM OF ACTION - Proton pump inhibitor; 5-HT1antagonist; calcium antagonist; angiotensin (II) antagonist.

USE - (A) is applied to the **nasal** mucosa (e.g. using a pump spray or valve spray, or as **nose** drops) for the **administration** of a wide range of (I) e.g. beclomethasone dipropionate, **scopolamine**, budesonide, diazepam or omeprazole.

ADVANTAGE - (II) adheres well to the **nasal** mucosa, spreads the cells and provides very good resorption of (I), with no pH dependency problems. The solutions of (I) are readily filtered (allowing easy sterilization by filtration), well tolerated/non-irritating (allowing good patient compliance) and highly stable; and do not support the growth of human-pathogenic microorganisms. The use of (environmentally harmful) propellants and (potentially allergenic) preservatives is avoided.
Dwg.0/0

L34 ANSWER 22 OF 28 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-041263 [05] WPIDS
DOC. NO. CPI: C2001-012028
TITLE: Composition for **intranasal administration** of water-insoluble drugs, e.g. **scopolamine**, budesonide or diazepam, comprising a solution of the water-insoluble or sparingly water-soluble drug in a neutral oil e.g. a triglyceride.
DERWENT CLASS: A96 B01 B02 B04 B05 B07
INVENTOR(S): KLOECKER, N
PATENT ASSIGNEE(S): (HEXA-N) HEXAL AG
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000074651	A1	20001214	(200105)*	GE	19

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

DE 19936543 A1 20010208 (200109)

AU 2000053973 A 20001228 (200119)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000074651	A1	WO 2000-EP4799	20000526
DE 19936543	A1	DE 1999-19936543	19990803
AU 2000053973	A	AU 2000-53973	20000526

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000053973	A	Based on	WO 200074651

PRIORITY APPLN. INFO: DE 1999-19936543 19990803; DE 1999-19925290 19990602

AN 2001-041263 [05] WPIDS

AB WO 200074651 A UPAB: 20010124

NOVELTY - A pharmaceutical composition (A) for **intranasal administration** comprises a solution of at least one water-insoluble or sparingly water-soluble active agent (I) in neutral oil (II).

USE - For the **intranasal administration** of water-insoluble or sparingly water-soluble drugs. (A) is applied to the **nasal** mucosa for the **administration** of a wide range of (I), e.g. beclomethasone dipropionate, **scopolamine**, budesonide, diazepam or omeprazole.

ADVANTAGE - (II) adheres well to the **nasal** mucosa, spreads the cells and provides very good resorption of (I), with no pH dependency problems. The solutions of (I) are readily filtered (allowing easy sterilization by filtration), well tolerated/non-irritating (allowing good patient compliance), highly stable and do not support the growth of human-pathogenic microorganisms. An exact dose is delivered. The use of (environmentally harmful) propellants and (potentially allergenic)

preservatives is avoided.
Dwg.0/0

L34 ANSWER 23 OF 28 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991-187335 [26] WPIDS
DOC. NO. CPI: C1991-081103
TITLE: New ACE-inhibitor aza bi cycloalkane amino acid derivs. - useful for treatment of arterial hypertension, ageing, senile dementia, etc..
DERWENT CLASS: B02
INVENTOR(S): HERVE, Y; LEPAGNOL, J; PORTEVIN, B; REMOND, G; VINCENT, M
PATENT ASSIGNEE(S): (ADIR) ADIR & CIE
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 434560	A	19910626	(199126)*		
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
AU 9068234	A	19910627	(199133)		
CA 2032735	A	19910621	(199135)		
FR 2655989	A	19910621	(199135)		
PT 96254	A	19910930	(199142)		
ZA 9009766	A	19910925	(199145)		
US 5151432	A	19920929	(199242)		10
JP 05320131	A	19931203	(199402)		15
EP 434560	B1	19940126	(199404)	FR	47
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
DE 69006338	E	19940310	(199411)		
ES 2062469	T3	19941216	(199505)		
JP 07121908	B2	19951225	(199605)		14
IE 66009	B	19951129	(199606)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 434560	A	EP 1990-403687	19901220
FR 2655989	A	FR 1989-16881	19891220
ZA 9009766	A	ZA 1990-9766	19901205
US 5151432	A	US 1990-629823	19901219
JP 05320131	A	JP 1990-403919	19901219
EP 434560	B1	EP 1990-403687	19901220
DE 69006338	E	DE 1990-606338	19901220
		EP 1990-403687	19901220
ES 2062469	T3	EP 1990-403687	19901220
JP 07121908	B2	JP 1990-403919	19901219

IE 66009 B IE 1990-4586 19901219

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 69006338	E	Based on	EP 434560
ES 2062469	T3	Based on	EP 434560
JP 07121908	B2	Based on	JP 05320131

PRIORITY APPLN. INFO: FR 1989-16881 19891220

AN 1991-187335 [26] WPIDS

AB EP 434560 A UPAB: 19930928

Substd. amino acid derivs (I) and their addn. salts with acids or bases are new. In (I) R1 = alkoxy, or NH2 opt. substd. with 1 or 2 1-6C alkyl gps; R2 = 1-6C alkyl opt. substd. by NH2; R3 = amino, alkoxy or OH gp; at least one amino group is present in R1 or R3; R4 = H or aryl; m = 1 or 2; n = 1-6; Ra and Rb = when m = 1, H when m = 2, H or 1-6C alkyl.

Prepn. of (I) comprises reductive amination of R3'-CO-CO-(CH2)n-R4 (II) in presence of a mixed hydride of an alkali metal e.g. sodium cyanoborohydride with an amino acid P-OCO-CH(R'2)-NH2 (III) having a protected acidic function. In (II) and (III) R'3 = amino or 1-6C alkoxy; P = alkyl e.g. tertbutyl; R'2 = 1-6C alkyl opt. substd. by an amino gp. itself protected by a protecting gp. (such as benzyloxycarbonyl) to obtain P-OCO-CH(R'2)-NH-CH(COR'3)-(CH2)n-R4 (IV). The isomers are sepd. and the compound is deprotected in acidic medium to obtain HO2C-CH(R'2)-NH-CH(COR'3)-(COR'3)-(CH2)n-R4 (V) which is then coupled with (VI) to obtain (IA). (Ia) is (I) where R2 = R'2 and R3 = R'3.

Pharmaceutical compsns. contg. (I) are also claimed.

(I) are pref. **administered** orally, parenterally or **nasally** in the form of tablets, sachets, capsules, suppositories, creams, ointments, etc. A typical dosage is 0.1-100 mg in 1-3 doses per 24 hrs.

USE/ADVANTAGE - (I) inhibit angiotensin I conversion enzyme and have antagonist effect on **scopolamine** induced amnesia. They are used to treat arterial hypertensive disease, and neurobehavioural disorders associated with cerebrovascular disorders, ageing and (pre)senile degenerative dementia such as Alzheimer's disease, Pick's disease multi-infarctus dementia and Binswangers disease. @(30pp Dwg.No.0/0)@

ABEQ US 5151432 A UPAB: 19930928

Substd. aminoacids, their enantiomers, diastereoisomers, epimers, and addn. salts with pharmaceutically acceptable acid or base are claimed and comprise of formula (I). In (I), R1 = (un)branched 1-6C or 7-12C chain alkoxy- or amino opt. substd. with at least one opt. branched 1-6C alkyl gps.; R2 = (un)branched 1-6C alkyl opt. substd.

with amino; R3 = amino, (un)branched 1-6C or 7-12C alkoxy or hydroxy with the proviso that at least one amino is present in R1 or ; R4 = H or Ph; m = 1 or 2; n = 1-6; and Ra and Rb independently = H whem m = 1 or (un)branched 1-6C alkyl or H when m = 2.

USE/ADVANTAGE - (I) are memory enhancers and are used to treat neuro-behavioural disorders associated with stroke, ageing, senile or pre-senile dementia such as Alzheimer's disease, Pick's disease, multi-infarct dementia and Binswanger's disease.

0/0

ABEQ EP 434560 B UPAB: 19940307

Compounds of the general formula (I) wherein: R1 represents a straight-chain or branched lower or higher alkoxy group, or an amino group optionally substituted by one or two straight-chain or branched lower alkyl groups; R2 represents a straight-chain or branched lower alkyl group optionally substituted by an amino group; R3 represnts an amino group, a straight-chain or branched lower or higher alkoxy group or a hydroxy group, with the proviso that at least one amino group is present in R1 or R3; R4 represents a hydrogen atom or an aryl group; m is 1 or 2; n is from 1 to 6; Ra and Rb, which are the same or different, represent a hydrogen atom when m = 1 and a straight-chain or branched lower alkyl group or a hydrogen atom when m = 2, the term ''lower'' denoting that groups so qualified contain from 1 to 6 carbon atoms, the term ''higher'' denoting that groups so qualified contain from 7 to 12 carbon atoms, their enantiomers, diastereoisomers and epimers, and also their addition salts with a pharmaceutically acceptable acid or base.

Dwg. 0/0

L34 ANSWER 24 OF 28 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991-119405 [17] WPIDS
CROSS REFERENCE: 1996-039530 [04]; 1997-331533 [30]; 1998-361764 [31]; 1999-033471 [03]; 1999-418286 [35]
DOC. NO. CPI: C1991-051433
TITLE: Use of anti-cholinergic agents which cross blood-brain barrier - for reducing neurotoxic effects of N-methyl-D-aspartate antagonists.
DERWENT CLASS: B05
INVENTOR(S): OLNEY, J W
PATENT ASSIGNEE(S): (OLNE-I) OLNEY J W
COUNTRY COUNT: 11
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 424179	A	19910424	(199117)*	EN	27

R: AT BE CH DE FR GB IT LI LU NL SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 424179	A	EP 1990-311526	19901019

PRIORITY APPLN. INFO: US 1990-467139 19900118; US 1989-424548 19891020

AN 1991-119405 [17] WPIDS

CR 1996-039530 [04]; 1997-331533 [30]; 1998-361764 [31]; 1999-033471 [03]; 1999-418286 [35]

AB EP 424179 A UPAB: 19990902

The use of an anti-cholinergic agent capable of penetrating the blood-brain barrier is claimed. The agent exerts an antagonistic effect on cholinergic receptors of the muscarinic type on the surfaces of neurons in the central nervous system and reduces the neurotoxic effects of an N-methyl-D-aspartate (NMDA) antagonists. A preferential effect is seen on type M1 receptors as opposed to type 2. The anti-cholinergic agent is **scopolamine**, atropine, benzotropine, benactyzine, biperiden, triperiden, procyclidine, trihexylphenidyl or diphenhydramine. An NMDA antagonist may be present in the packaging material contg. the anti-cholinergic agent. A non-NMDA antagonist may be used e.g. quinoxalinedione. **Administration** is e.g. oral, intravenous, intramuscular, subcutaneous, intradermal, **nasal**, topical, buccal or sublingual. Dosage of **scopolamine** at 0.25 mg/kg. was totally effective in test animals.

USE/ADVANTAGE - The NMDA antagonist is used to reduce deleterious neurological effects - they reduce excitotoxic damage in the brain and the anti-cholinergic agent reduces one or more of the neurotoxic effects. The central nervous system is the protected against neurotoxic side effects of certain drugs and neurodegenerative diseases. Conditions prevented includer hypoglycaemia, hypoxia, ischaemia, persistent seizure, trauma, thiamine deficiency, methamphetamine poisoning, alcoholism and related conditions, Creutzfeldt-Jakob syndrome and encephalitis associated with herpes or measles.

Dwg.0/0

ABEQ US 5034400 A UPAB: 19930928

Reducing the neurotoxic effects of an NMDA antagonist comprises **admin.**, in conjunction with the NMDA antagonist, of an anti-cholinergic agent which penetrates the blood-brain barrier in a therapeutically effective quantity sufficient to exert a pharmaceutically antagonistic effect on cholinergic receptors of the muscarinic type on the surfaces of neurons in the CNS.

The NMDA antagonist is pref. MK-801, phencyclidine, ketomine or tiletamine.

USE/ADVANTAGE - The agents reduce or eliminate deleterious side

effects that can accompany NMDA antagonists without interfering with useful properties of the NMDA antagonists. The agents also reduce the neurotoxic, psychotoxic and/or hallucinatory side effects associated with drugs such as phencyclidine.

ABEQ US 5616580 A UPAB: 19970512
A pharmacological compsn. comprises a mixt. of an NMDA antagonist and an anti-cholinergic agent, both of which can penetrate blood-brain barriers, wherein the NMDA antagonist is present in a therapeutically effective quantity sufficient to reduce excitotoxic damage in the brain if **administered** to a mammal, and wherein the NMDA antagonist can cause neurotoxic side effects in the brain if **administered** without an accompanying anti-cholinergic agent, and wherein the anti-cholinergic agent is present in a second quantity that can reduce the neurotoxic side effects which would be caused by the NMDA antagonist if **administered** without the accompanying anti-cholinergic agent.
Dwg.0/0

L34 ANSWER 25 OF 28 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1991-052209 [08] WPIDS
DOC. NO. CPI: C1991-022177
TITLE: Storage stable soln. of alkaloid, esp. atropine - contg. water absorbent beads, esp. mol. sieve, partic. for use in aerosols to deliver very precise doses.
DERWENT CLASS: B02
INVENTOR(S): LETTKO, H
PATENT ASSIGNEE(S): (AERO-N) AEROCHEM H LETTKO
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 3926751	A	19910214	(199108)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 3926751	A	DE 1989-3926751	19890812

PRIORITY APPLN. INFO: DE 1989-3926751 19890812
AN 1991-052209 [08] WPIDS
AB DE 3926751 A UPAB: 19930928
Storage stable alcoholic soln. of alkaloids (A), e.g. atropine, **scopolamine**, L-hyoscyamine, their quat. ammonium cpds. and

atropine-like cpds., contains a porous, adsorbent crystalline powder (B) in bead form.

More specifically (B) is molecular sieve, esp. crystalline alkali or alkaline earth aluminosilicate of pore size 3-4 Angstroms and pref. mean particle size 1.5-1.7 mm.

USE/ADVANTAGE - These solns. have parasympatholytic properties and can be **admin**. intravenously, intramuscularly, oral, by inhalation or esp. as a **nasal** spray, e.g. for treatment of poisoning by alkylphosphates (insecticides or war gases). Addn. of (B), which absorbs water but is inert towards (A) and solvent, improves stability of the soln. such that it can be stored for at least a year. This soln. can be delivered in exact doses from aerosols.

0/0

L34 ANSWER 26 OF 28 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:627199 SCISEARCH
THE GENUINE ARTICLE: 109RN
TITLE: Effects of antidepressant treatment on inhibitory avoidance behavior and amygdaloid beta-adrenoceptors in rats
AUTHOR: Daws L C (Reprint); Lopez R; Frazer A
CORPORATE SOURCE: UNIV TEXAS, HLTH SCI CTR, DEPT PHARMACOL, 7703 FLOYD CURL DR, SAN ANTONIO, TX 78284 (Reprint); S TEXAS VET HLTH CARE SYST, AUDIE L MURPHY MEM VET HOSP, SAN ANTONIO, TX
COUNTRY OF AUTHOR: USA
SOURCE: NEUROPSYCHOPHARMACOLOGY, (OCT 1998) Vol. 19, No. 4, pp. 300-313.
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010.
ISSN: 0893-133X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 60

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Chronic treatment of mts with a variety of antidepressants results in the down-regulation of beta(1)-adrenoceptors ill the amygdaloid nuclei. The present study sought to determine if this specific neurochemical effect caused air alteration in inhibitory az,avoidance conditioning, a behavior considered to be mediated by beta-adrenoceptors in the amygdala. Rats treated chronically with either desipramine (DMI) or phenelzine (PHEN), which down-regulate beta(1)-adrenoceptors in the amygdala, or fluoxetine (FLUOX), which does not no this, did not exhibit a deficit in the retention of the inhibitory avoidance task. However, when **scopolamine** was given prior to acquisition of the task in a **nose** that, by

itself, did not affect retention, DMI- and PHEN-treated rats showed a marked deficit in retention. This effect was also observed after acute **administration** of these drugs, although they did not down-regulate amygdaloid beta(1)-adrenoceptors at this time. It seems that the ability of these antidepressants to potentiate the amnesic effect of **scopolamine** is unrelated to their effect on beta(1)-adrenoceptor number in the amygdala and that the extent of antidepressant-induced amygdaloid beta(1)-adrenoceptor down-regulation is not sufficient, by itself, to cause a deficit in an inhibitory avoidance task. (C) 1998 American College of Neuropsychopharmacology. Published by Elsevier Science Inc.

L34 ANSWER 27 OF 28 JICST-EPlus COPYRIGHT 2001 JST

ACCESSION NUMBER: 970605077 JICST-EPlus

TITLE: Fiberoptoic Nasotracheal Intubation for Mandibular Micrognathia with the Aid of Nasopharyngeal Tube: A Case Report.

AUTHOR: FUKUDA KEN'ICHI; SUGIYAMA AYAKO; ICHINOHE TATSUYA; KANEKO YUZURU

CORPORATE SOURCE: Tokyo Dent. Coll.

SOURCE: Nippon Rinsho Masui Gakkaishi (Journal of Japan Society for Clinical Anesthesia), (1997) vol. 17, no. 5, pp. 328-331. Journal Code: Y0691A (Fig. 2, Ref. 15)
ISSN: 0285-4945

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Short Communication

LANGUAGE: Japanese

STATUS: New

AB We anesthetized a 6-yaer-old boy with mandibular micrognathia and microstomia undergoing surgical implantaion of Hoffman mini-expanders. Retrograde intubation and insertion of a laryngeal mask was impossible because of trismus and microstomia. Couscious intubation was also difficult because of the patient's age. Accordingly, we selected fiberoptoic nasotracheal intubation under inhaled anesthesia with a nasopharygeal tube. After premedication with intramuscular **scopolamine**, anesthesia was induced with intravenous midazolam and ketamine. Care was taken not to depress the patient's spontaneous ventilation. After an adequate topical anesthesia of the nasopharyngeal area, a **nasal** airway was inserted into the right **nostril**. Then, the patient was **administered** 50% nitrous oxide, 3% sevoflurane and oxygen by inhalation via the airway. After attaining an adequate depth of anesthesia, a transtracheal topical anesthesia in the larynx and the trachea was performed. Fiberoptoic nasotracheal intubation through the left **nostril** was completed readily and safely with this method. (author abst.)

L34 ANSWER 28 OF 28 JICST-EPlus COPYRIGHT 2001 JST
ACCESSION NUMBER: 880406262 JICST-EPlus
TITLE: A female pediatric case of postoperative atelectasis with intermaxillary fixation.
AUTHOR: YAMADA MORIMASA; ARAI TOYOHISA; ABE ASAKO; AOYAMA TATSUKO; SATOH KOJI; TSUJIKAWA TAKAAKI; HIBI GORO
CORPORATE SOURCE: Fujita-Gakuen Health Univ., School of Medicine
SOURCE: Nippon Shika Masui Gakkai Zasshi (Journal of Japanese Dental Society of Anesthesiology), (1988) vol. 16, no. 2, pp. 273-278. Journal Code: Y0016A (Fig. 7, Ref. 17)
ISSN: 0386-5835
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Short Communication
LANGUAGE: Japanese
STATUS: New
AB We report on a 8-year-old female patient with the maxillary, zygomatic, **nasal**, and orbital fractures (Le Fort III type) suffered in a traffic accident. The patient was operated on for repair of the fractures one week after the accident. As premedication, **scopolamine** and hydroxyzine were **administered** by intramuscular injection one hour before the operation, and she was anesthetized with inhalation of nitrous oxide, oxygen, and halothane. During and after the operatin, no unfavorable phenomena were observed, but her postoperative condition changed suddenly three days after the operation. Atelectasis of the left lung was found by chest X-ray, and we aspirated a great of quantity of bronchial secretion by fiberscope under general anesthesia and began respiratory management (PEEP, SIMV) by SERVO VENTILATOR 900B. The atelectasis of her left lung was eliminated by lung physiotherapy (respiration exercise, cough exercise, trapping, vibration, postural drainage), early rising, suction, aerosol nebulizing therapy, and chemotherapy. The patient was discharged from our hospital thirty-six days after her admission. In such a case early diagnosis and adequate treatment are important.(author abst.)

FILE 'HOME' ENTERED AT 10:52:24 ON 07 MAY 2001

Jiang, S.
09/486839

(FILE 'REGISTRY' ENTERED AT 10:20:02 ON 07 MAY 2001)
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SCOPOLAMINE/CN
L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON "SCOPOLAMINE BROMIDE"/C N
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2

(FILE 'CAPLUS' ENTERED AT 10:20:28 ON 07 MAY 2001)
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SCOPOLAMINE/CN
L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON "SCOPOLAMINE BROMIDE"/C N
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2
L4 6773 SEA FILE=CAPLUS ABB=ON PLU=ON L3 OR SCOPOLAMINE OR SCOPOL AMINE
L5 140 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND (NAUSEA? OR VOMIT? OR (MOTION OR AIR OR CAR OR SEA)(W)SICKNESS OR AIRSICKNESS OR CARSICKNESS OR SEASICKNESS OR EMESIS)
L7 5 SEA FILE=CAPLUS ABB=ON PLU=ON L5 AND (NASAL? OR NOSE OR RHINO? OR INTRANASAL? OR NOSTRIL)

L7 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:259923 CAPLUS
TITLE: **Scopolamine nasal** spray in **motion sickness**: a randomised, controlled, and crossover study for the comparison of two **scopolamine nasal** sprays with oral dimenhydrinate and placebo
AUTHOR(S): Klocker, N.; Hanschke, W.; Toussaint, S.; Verse, T.
CORPORATE SOURCE: Muhlfeldstr. 22, AUDIT Institute for Medical Services and Quality Assurance, 65232, Taunusstein, Germany
SOURCE: Eur. J. Pharm. Sci. (2000), 13(2), 227-232
CODEN: EPSCED; ISSN: 0928-0987
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Scopolamine** has been used successfully for treatment of **motion sickness** for almost a century and the **nasal** administration was first studied 50 yr ago. However, there never appeared a **nasal** dosage form. Finally, after finding a stable and suitable formulation for **scopolamine**, a study to investigate efficacy, safety, and tolerability was conducted, with a randomised, double-blind, double-dummy, crossover, Latin square design including placebo control and a placebo/placebo control for internal validity at the German Air Force Institute of Aviation Medicine. To assess the efficacy of a new, stable and well-tolerated formulation of **scopolamine nasal**

spray the reproducible induction of whole body vibrations by a rotating chair was chosen and a validated **seasickness** score (SKS). The redn. of SKS showed that **scopolamine** **nasal** spray at a concn. of 0.2% was statistically superior to both placebo and dimenhydrinate (P=0.003 and 0.004, resp.). There were no signs for a **nasal** or epipharyngeal irritation of the mucous membrane. **Scopolamine** **nasal** spray was found to be an effective and safe treatment in **motion sickness**, with a fast onset of action within 30 min after administration.

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:700676 CAPLUS
DOCUMENT NUMBER: 134:9249
TITLE: Effects of pH and dose on **nasal** absorption of **scopolamine** hydrobromide in human subjects
AUTHOR(S): Ahmed, Shamim; Sileno, Anthony P.; DeMeireles, Jorge C.; Dua, Ramneik; Pimplaskar, Harish K.; Xia, Wei J.; Marinaro, John; Langenback, Edward; Matos, Frank J.; Putcha, Lakshmi; Romeo, Vincent D.; Behl, Charan R.
CORPORATE SOURCE: Nastech Pharmaceutical Company, Inc., Hauppauge, NY, 11788, USA
SOURCE: Pharm. Res. (2000), 17(8), 974-977
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was conducted to evaluate the effects of formulation pH and dose on **nasal** absorption of **scopolamine** hydrobromide, the single most effective drug available for the prevention of **nausea** and **vomiting** induced by **motion sickness**. Human subjects received **scopolamine** **nasally** at a dose of 0.2 mg/0.05 mL or 0.4 mg/0.10 mL, blood samples were collected at different time points, and plasma **scopolamine** concns. were detd. by LC-MS/MS. Following administration of a 0.2 mg dose, the av. Cmax values were found to be 262 .+-. 118, 419 .+-. 161, and 488 .+-. 331 pg/mL for pH 4.0, 7.0, and 9.0 formulations, resp. At the 0.4 mg dose the av. Cmax values were found to be 503 .+-. 199, 933 .+-. 449, and 1,308 .+-. 473 pg/mL for pH 4.0, 7.0, and 9.0 formulations, resp. At a 0.2 mg dose, the AUC values were found to be 23,208 .+-. 6,824, 29,145 .+-. 9,225, and 25,721 .+-. 5,294 pg.min/mL for formulation pH 4.0, 7.0, and 9.0, resp. At a 0.4 mg dose, the av. AUC value was found to be high for pH 9.0 formulation (70,740 .+-. 29,381 pg.min/mL) as compared to those of pH 4.0 (59,573 .+-. 13,700 pg.min/mL) and pH 7.0 (55,298 .+-. 17,305

pg.min/mL) formulations. Both the Cmax and AUC values were almost doubled with doubling the dose. On the other hand, the av. Tmax values decreased linearly with a decrease in formulation pH at both doses. For example, at a 0.4 mg dose, the av. Tmax values were 26.7 .+-. 5.8, 15.0 .+-. 10.0, and 8.8 .+-. 2.5 min at formulation pH 4.0, 7.0, and 9.0, resp. **Nasal** absorption of **scopolamine** hydrobromide in human subjects increased substantially with increases in formulation pH and dose.

IT **51-34-3, Scopolamine 114-49-8,** **Scopolamine** hydrobromide
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(effects of pH and dose on **nasal** absorption of **scopolamine** hydrobromide in human subjects)

REFERENCE COUNT: 17
REFERENCE(S):
(2) Chien, Y; Critical Reviews in Therapeutic Drug Career Systems 1987, P67 CAPLUS
(4) Cintron, N; J Pharm Sci 1987, V76, P328 CAPLUS
(7) Hirai, S; Diabates 1978, V27, P296 CAPLUS
(8) Hussain, A; Transnasal Systemic Medications 1985, P121 CAPLUS
(10) Kagatani, S; Pharm Res 1998, V15, P77 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:193998 CAPLUS
DOCUMENT NUMBER: 130:227753
TITLE: **Intranasal** formulation containing **scopolamine** for the treatment of **motion sickness**
INVENTOR(S): Achari, Raja G.; Behl, Charanjit R.; Chowhan, Prafulla K.; De Meireles, C. Jorge; Dua, Ramneik; Romeo, Vincent D.; Sileno, Anthony P.
PATENT ASSIGNEE(S): Nastech Pharmaceutical Company, Inc., USA; De Meireles, C. Jorge
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912544	A1	19990318	WO 1998-US18953	19980911

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9893850	A1	19990329	AU 1998-93850	19980911
EP 1027049	A1	20000816	EP 1998-946945	19980911

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1997-58651 P 19970911
WO 1998-US18953 W 19980911

AB The present invention relates to pharmaceutical formulations contg. **scopolamine**. More particularly, the invention relates to an **intranasal** gel formulation including **scopolamine** hydrobromide (I) in a pharmaceutically acceptable carrier, most preferably an **intranasal** gel, at a pH at or below about 4.0, preferably at or below about 3.5, and a salt concn. below about 200 mM, with the gel soln. incorporating polyvinylalc. as a gelling agent. The **intranasal** formulations are particularly useful for preventing and/or treating **nausea** and/or **vomiting** assocd. with, for example, **motion sickness**. A gel contained I 0.2, citric acid 0.37, sodium citrate dihydrate 0.17, sodium metabisulfite 0.1, glycerin 5.0, Me cellulose 2.0, benzalkonium chloride 0.04 g, and water q.s. 100 mL. The gel was stable after storage at 40.degree. and 75% humidity over 6 mo period.

IT **51-34-3, Scopolamine 114-49-8, Scopolamine** hydrobromide
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**intranasal** formulation contg. **scopolamine** for treatment of **motion sickness**)

REFERENCE COUNT: 2
REFERENCE(S):
(1) Osol; Remington's Pharmaceutical Sciences 1975, V15th Ed, P1242
(2) Putcha, L; US 765615 A0 Intranasal Scoploamine Preparation 1992 CAPLUS

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:241967 CAPLUS
DOCUMENT NUMBER: 116:241967
TITLE: **Intranasal scopolamine** preparation
INVENTOR(S): Putcha, Lakshmi; Cintron, Nitza M.

PATENT ASSIGNEE(S): United States National Aeronautics and Space Administration, USA
SOURCE: U. S. Pat. Appl., 11 pp. Avail. NTIS Order No. PAT-APPL-7-765,615.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 765615	A0	19920315	US 1991-765615	19910925

AB A method and prepn. for **intranasal scopolamine** (I) delivery provides a safe and effective treatment for **motion sickness** and other conditions requiring anti-cholinergic therapy. The prepn. can be in the form of aq. **nasal** drops, mist spray, gel, or ointment. **Intranasal** delivery of I has similar bioavailability and effect of i.v. delivery and is far superior to oral dosage. Bioavailability data for i.v., oral, and **intranasal** I are included.

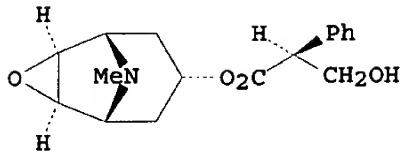
IT **51-34-3, Scopolamine**
RL: BIOL (Biological study)
(**intranasal** pharmaceutical of)

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:166916 CAPLUS
DOCUMENT NUMBER: 98:166916
TITLE: **Motion sickness** **nasal** spray
INVENTOR(S): Keith, Alec Dell
PATENT ASSIGNEE(S): Key Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8300286	A1	19830203	WO 1982-US941	19820712
W: JP				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
EP 83373	A1	19830713	EP 1982-902562	19820712
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
JP 58501129	T2	19830714	JP 1982-502527	19820712

PRIORITY APPLN. INFO.: US 1981-283447 19810715
WO 1982-US941 19820712

GI



I

AB An aerosol spray is prepd. by dissolving 1 mg **scopolamine** (I) [**51-34-3**] in 99.9 mL 20% EtOH, and 15 mL of the soln. is packaged in a 4-way spray container. Spraying .apprx.50 mg of the compn. (.apprx.100 .mu.g I) into each **nostril** provided rapid and sustained (.apprx.3h) relief from **motion sickness**.

IT **51-34-3**
RL: BIOL (Biological study)
(**nasal** spray contg., for **motion sickness** treatment in humans)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:28:48 ON 07 MAY 2001)
L8 24 S L7
L9 17 DUP REM L8 (7 DUPLICATES REMOVED)

L9 ANSWER 1 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001136878 EMBASE
TITLE: **Scopolamine nasal** spray in **motion sickness**: A randomised, controlled, and crossover study for the comparison of two **scopolamine nasal** sprays with oral dimenhydrinate and placebo.
AUTHOR: Klocker N.; Hanschke W.; Toussaint S.; Verse T.
CORPORATE SOURCE: N. Klocker, AUDIT Institute Medical Service, Quality Assurance, Muhlfeldstr. 22, 65232 Taunusstein, Germany. audit.institute@t-online.de
SOURCE: European Journal of Pharmaceutical Sciences, (2001) 13/2 (227-232).
Refs: 23
ISSN: 0928-0987 CODEN: EPSCED
PUBLISHER IDENT.: S 0928-0987(01)00107-5
COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 011 Otorhinolaryngology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Scopolamine** has been used successfully for treatment of **motion sickness** for almost a century and the **nasal** administration was first studied 50 years ago. However, there never appeared a **nasal** dosage form. Finally, after finding a stable and suitable formulation for **scopolamine**, a study to investigate efficacy, safety, and tolerability was conducted, with a randomised, double-blind, double-dummy, crossover, Latin square design including placebo control and a placebo/placebo control for internal validity at the German Air Force Institute of Aviation Medicine. To assess the efficacy of a new, stable and well-tolerated formulation of **scopolamine nasal** spray the reproducible induction of whole body vibrations by a rotating chair was chosen and a validated **seasickness** score (SKS). The reduction of SKS showed that **scopolamine nasal** spray at a concentration of 0.2% was statistically superior to both placebo and dimenhydrinate (P=0.003 and 0.004, respectively). There were no signs for a **nasal** or epipharyngeal irritation of the mucous membrane. **Scopolamine nasal** spray was found to be an effective and safe treatment in **motion sickness**, with a fast onset of action within 30 min after administration. Copyright .COPYRGT. 2001 Elsevier Science B.V.

L9 ANSWER 2 OF 17 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000477574 MEDLINE
DOCUMENT NUMBER: 20479915 PubMed ID: 11028944
TITLE: Effects of pH and dose on **nasal** absorption of **scopolamine** hydrobromide in human subjects.
AUTHOR: Ahmed S; Sileno A P; deMeireles J C; Dua R; Pimplaskar H K; Xia W J; Marinaro J; Langenback E; Matos F J; Putcha L; Romeo V D; Behl C R
CORPORATE SOURCE: Nastech Pharmaceutical Company, Inc., Hauppauge, New York 11788, USA.
SOURCE: PHARMACEUTICAL RESEARCH, (2000 Aug) 17 (8) 974-7. Journal code: PHS. ISSN: 0724-8741.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010209
Entered Medline: 20010215

AB PURPOSE: The present study was conducted to evaluate the effects of formulation pH and dose on **nasal** absorption of **scopolamine** hydrobromide, the single most effective drug available for the prevention of **nausea** and **vomiting** induced by **motion sickness**.
METHODS: Human subjects received **scopolamine** **nasally** at a dose of 0.2 mg/0.05 mL or 0.4 mg/0.10 mL, blood samples were collected at different time points, and plasma **scopolamine** concentrations were determined by LC-MS/MS.
RESULTS: Following administration of a 0.2 mg dose, the average Cmax values were found to be 262+/-118, 419+/-161, and 488+/-331 pg/ mL for pH 4.0, 7.0, and 9.0 formulations, respectively. At the 0.4 mg dose the average Cmax values were found to be 503+/-199, 933+/-449, and 1,308+/-473 pg/mL for pH 4.0, 7.0, and 9.0 formulations, respectively. At a 0.2 mg dose, the AUC values were found to be 23,208+/-6,824, 29,145+/-9,225, and 25,721+/-5,294 pg x min/mL for formulation pH 4.0, 7.0, and 9.0, respectively. At a 0.4 mg dose, the average AUC value was found to be high for pH 9.0 formulation (70,740+/-29,381 pg x min/mL) as compared to those of pH 4.0 (59,573+/-13,700 pg x min/mL) and pH 7.0 (55,298+/-17,305 pg x min/mL) formulations. Both the Cmax and AUC values were almost doubled with doubling the dose. On the other hand, the average Tmax, values decreased linearly with a decrease in formulation pH at both doses. For example, at a 0.4 mg dose, the average Tmax values were 26.7+/-5.8, 15.0+/-10.0, and 8.8+/-2.5 minutes at formulation pH 4.0, 7.0, and 9.0, respectively. CONCLUSIONS: **Nasal** absorption of **scopolamine** hydrobromide in human subjects increased substantially with increases in formulation pH and dose.

L9 ANSWER 3 OF 17 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-229134 [19] WPIDS
DOC. NO. CPI: C1999-067379
TITLE: **Scopolamine intranasal** formulation for treating **motion sickness**.
DERWENT CLASS: A18 A96 B02 B07
INVENTOR(S): ACHARI, R G; BEHL, C R; CHOWHAN, P K; DE MEIRELES, C J; DUA, R; ROMEO, V D; SILENO, A P
PATENT ASSIGNEE(S): (NAST-N) NASTECH PHARM CO INC
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 9912544 A1 19990318 (199919)* EN 40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9893850 A 19990329 (199932)
EP 1027049 A1 20000816 (200040) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9912544	A1	WO 1998-US18953	19980911
AU 9893850	A	AU 1998-93850	19980911
EP 1027049	A1	EP 1998-946945	19980911
		WO 1998-US18953	19980911

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9893850	A	Based on	WO 9912544
EP 1027049	A1	Based on	WO 9912544

PRIORITY APPLN. INFO: US 1997-58651 19970911
AN 1999-229134 [19] WPIDS
AB WO 9912544 A UPAB: 19990518
NOVELTY - An **intranasal** formulation comprises **scopolamine** in a carrier at a pH below 4.0 and a salt concentration below 200 mM, the carrier incorporating polyvinyl alcohol (PVA). The **scopolamine** may be in the form of a chemically modified equivalent or salt, especially the hydrobromide.
USE - The formulation is useful for preventing and/or treating **nausea** and/or **vomiting** associated with, eg. **motion sickness**.
ADVANTAGE - The formulation provides a therapeutically effective amount of **scopolamine** into the bloodstream over a short time period (30 minutes or less), provides effective levels over a sustained amount of time, does not degrade over time, and is not irritating to the **nasal** cavity.
Dwg.2/2

L9 ANSWER 4 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998285306 EMBASE

TITLE: Comparative tolerability of drug therapies used to treat incontinence and enuresis.
AUTHOR: Owens R.G.; Karram M.M.
CORPORATE SOURCE: Dr. M.M. Karram, Seton Center, Good Samaritan Hospital, 375 Dixmyth Avenue, Cincinnati, OH 45220, United States
SOURCE: Drug Safety, (1998) 19/2 (123-139).
Refs: 62
ISSN: 0114-5916 CODEN: DRSAEA
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Drug therapy for incontinence and enuresis has met with varying degrees of success. Currently, there is no medication available that specifically targets the lower urinary tract without having untoward effects elsewhere in the body. Patients with urge incontinence are the most difficult group to treat. The agents most commonly used to treat urge incontinence, i.e. anticholinergics, musculotropics and tricyclic antidepressants, are limited in their effectiveness and have anticholinergic adverse effects. Other medications with theoretical treatment potential such as nonsteroidal anti-inflammatory drugs and calcium antagonists require more in depth clinical study before widespread use is appropriate. Although estrogen is well tolerated, its role in the treatment of incontinence in postmenopausal women may be limited, Medical treatment for stress incontinence is most successful in patients with a mild condition. Drugs with .alpha.-adrenergic activity alone or in combination with estrogen in postmenopausal women, are fairly effective and demonstrate few adverse effects at doses used to treat stress incontinence. Enuresis pharmacotherapy consists mainly of desmopressin and tricyclic antidepressants. Adverse effects are minimal with the doses commonly used. While the majority of patients improve with therapy, a significant portion relapse after treatment is terminated. Tolerability of a particular therapy depends on the effectiveness and adverse effects of the agent, the severity of incontinence and the general health of the patient. In general, patients are willing to accept a greater degree of inconvenience if a drug produces the desired effect. However, individualisation of therapy should be used to maximise compliance and outcome. Blinded, dose-titration studies are needed to better determine doses for optimum tolerability. Research into drugs specifically targeting the lower urinary tract may lead to more effective and well tolerated therapy for incontinence and enuresis.

L9 ANSWER 5 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97274981 EMBASE
DOCUMENT NUMBER: 1997274981
TITLE: Optimisation of drug delivery: 2. Principles of drug delivery and limitations of conventional non-oral dosage forms.
AUTHOR: Benson H.A.E.; Prankerd R.J.
CORPORATE SOURCE: Dr. H.A.E. Benson, Department of Pharmacy, Steele Building, University of Queensland, St Lucia Old, QLD 4072, Australia. heather@pharmacy.uq.edu.au
SOURCE: Australian Journal of Hospital Pharmacy, (1997) 27/4 (313-320).
Refs: 29
ISSN: 0310-6810 CODEN: AUHPAI
COUNTRY: Australia
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The first article in this series outlined some common problems in the use of oral dosage forms and indicated some approaches to the solution of these problems. The present view addresses similar problems with traditional non-oral dosage forms. These routes of administration are generally used when a deficiency of the oral route prevents achievement of the desired drug effect when given by this route. Examples are when a very rapid response is required (e.g. induction of general anaesthesia, treatment of status epilepticus), local rather than systemic effect, or when **vomiting** prevents adequate oral absorption.

L9 ANSWER 6 OF 17 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 97196639 MEDLINE
DOCUMENT NUMBER: 97196639 PubMed ID: 9043729
TITLE: Anticholinergics improve fibreoptic intubating conditions during general anaesthesia.
AUTHOR: Brookman C A; Teh H P; Morrison L M
CORPORATE SOURCE: Department of Anaesthetics, St. John's Hospital at Howden, Livingston, Scotland.
SOURCE: CANADIAN JOURNAL OF ANAESTHESIA, (1997 Feb) 44 (2) 165-7.
Journal code: C8L; 8701709. ISSN: 0832-610X.
PUB. COUNTRY: Canada
(CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970523
Last Updated on STN: 19970523
Entered Medline: 19970515

AB PURPOSE: To determine if anticholinergic agents improve fibreoptic intubating conditions and to compare the efficacy and side effects of glycopyrrolate and hyoscine. METHODS: Eighty ASA I adults undergoing elective wisdom tooth extraction were randomly allocated to receive 0.4 mg hyoscine hydrobromide po, 0.4 mg hyoscine hydrobromide im, 0.4 mg glycopyrrolate im or no anticholinergic, one hour pre-operatively. All underwent **nasal** fibreoptic intubation under general anaesthesia. The time taken to pass the fibreoptic scope was noted and visual analogue scores (VAS) were recorded for clarity of visual field and post-operative sore throat, dry mouth and **nausea**. RESULTS: The time to intubation was not different among the four groups (Kruschal-Wallis P = 0.07). The clarity of visual field was improved in all three anticholinergic groups (Kruschal-Wallis P = 0.006), but there was no difference among the three groups (median VAS control 6.4, glycopyrrolate 8.0, oral hyoscine 7.9, im hyoscine 7.7). There was no difference in post-operative side effects among any of the groups at both 30 min and four hours. CONCLUSION: The addition of an anticholinergic produced better visual conditions for intubation but had no effect on the incidence of post-operative sore throat, dry mouth and **nausea**.

L9 ANSWER 7 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 3
ACCESSION NUMBER: 96249864 EMBASE
DOCUMENT NUMBER: 1996249864
TITLE: Bioavailability of **intranasal** **scopolamine** in normal subjects.
AUTHOR: Putcha L.; Tietze K.J.; Bourne D.W.A.; Parise C.U.; Hunter R.P.; Cintron N.M.
CORPORATE SOURCE: Biomedical Operations/Research Br., NASA-Johnson Space Center,Houston, TX 77058, United States
SOURCE: Journal of Pharmaceutical Sciences, (1996) 85/8 (899-902).
ISSN: 0022-3549 CODEN: JPMSAE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The bioavailabilily of **scopolamine** in three dosage forms was compared in 12 healthy nonsmoking male volunteers. Subjects received 0.4-mg doses of **scopolamine** bromide in intravenous (IV), **intranasal** (IN), or oral (PO) dosage forms on three occasions, with at least 2 weeks separating the doses. Scopelamine concentrations in plasma were determined with a combined reverse- phase liquid chromatographic-radioreceptor binding assay. Saliva volume and flow rate and percent suppression of control flow rate were determined from each sample. Absorption after IN and PO **scopolamine** administration was rapid; plasma concentrations [1680 (IN) and 164 pg/mL (PO)] peaked within 1 h of dosing [0.37 (IN) and 0.78 h (PO)], respectively. IN and IV **scopolamine** suppressed salivary flow rate to similar extents (95% and 99.7%), respectively. Times to reach maximum effect were 1.05 and 0.27 h after IN and IV dosage, respectively. Absolute **intranasal** bioavailability, calculated from the area under the drug concentration vs time curve, was found to be significantly greater than that of PO **scopolamine** (83% vs 3.7%, $p < 0.05$). The IN route may provide a noninvasive, reliable, fast, and effective route for administering **scopolamine**.

L9 ANSWER 8 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96090850 EMBASE
DOCUMENT NUMBER: 1996090850
TITLE: Risks and benefits of drugs used in the management of postoperative **nausea** and **vomiting**
.
AUTHOR: Sung Y.-F.
CORPORATE SOURCE: Ambulatory Surgery Center, The Emory Clinic, 1365-B Clifton Road,NE Atlanta, United States
SOURCE: Drug Safety, (1996) 14/3 (181-197).
ISSN: 0114-5916 CODEN: DRSAEA
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
024 Anesthesiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Postoperative **nausea** and **vomiting** (PONV) is an age-old problem; more so since the blooming of ambulatory or day surgery centres within the last 2 decades. The aetiology of PONV is multifactorial. The incidence of PONV is usually higher in women and children than in men. PONV not only causes patient discomfort, anxiety in mild cases, and serious complications in severe cases, it also decreases cost efficiency. The benefits and risks of old and new antiemetic drugs used worldwide to treat PONV are discussed in

this article, including the newly developed serotonin 5-hydroxytryptamine 3 (5HT3) antagonists. All the medications currently used to treat PONV have both advantages and disadvantages. If used indiscriminately to treat patients who have no problems with PONV, the risks of adverse effects often outweigh the benefits. The patient's history and the nature of the surgery are good indicators for defining those at risk from PONV; for patients at risk preventive treatment is essential. However, it is almost impossible to pick one agent or one combination as the therapy of choice using the present available data. A patient history of a favourable response to a previously used antiemetic would make that drug the agent of choice. So far, the newcomers, the 5HT3 antagonists, have fewer reported adverse effects.

L9 ANSWER 9 OF 17 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:211184 BIOSIS
DOCUMENT NUMBER: PREV199598225484
TITLE: Rectal versus intramuscular morphine-**scopolamine** as premedication in children.
AUTHOR(S): Guldbrand, Pehr (1); Mellstrom, A.
CORPORATE SOURCE: (1) Dep. Anaesthesiol., Falu Hosp., S-791 82 Falun Sweden
SOURCE: Acta Anaesthesiologica Scandinavica, (1995) Vol. 39, No. 2, pp. 224-227.
ISSN: 0001-5172.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Intramuscular morphine-**scopolamine** for premedication was compared with a hydrogel of the same drugs for rectal administration in 205 healthy children scheduled for minor ENT surgery. The intramuscular dose was 0.15 +- 0.006 mg times kg-1 compared to 0.25 +- 0.015 mg times kg-1 rectally. Reaction at administration and anaesthetic induction, incidence of intraoperative air-way difficulties, SpO-2, ECG changes, postoperative pain and incidence of **nausea** were recorded. The administration for the rectal hydrogel group worked better and resulted in less postoperative **nausea** and slightly more postoperative pain. The children's behaviour at anaesthesia induction and the frequency of perioperative complications were similar in both groups. We conclude that for minor ENT surgery on children, premedication with rectal hydrogel of morphine-**scopolamine** is a good alternative to intramuscular morphine-**scopolamine**.

L9 ANSWER 10 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95028333 EMBASE
DOCUMENT NUMBER: 1995028333
TITLE: The combination of tizanidine markedly improves the treatment with dextromethorphan of heroin addicted

outpatients.

AUTHOR: Koyuncuoglu H.
CORPORATE SOURCE: Pharmacology Clinical Pharmacology, Istanbul Medical Faculty,34390 Capa-Istanbul, Turkey

SOURCE: International Journal of Clinical Pharmacology and Therapeutics, (1995) 33/1 (13-19).
ISSN: 0174-4879 CODEN: ICTHEK
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB According to the hypothesis implying that the main mechanism underlying opiate addiction is the blockade by opiates of NMDA receptor functions and subsequent upregulation and supersensitivity of the receptors, noncompetitive NMDA receptor blocker dextromethorphan (DM) has been successfully used in the heroin addict treatment. As the stimulation of NMDA receptors modulates the release of neurotransmitters and hormones such as NE, D, ACh, GH, LH, LSH, ACTH etc., all of which have been found responsible for the manifestation of abstinence syndrome signs including craving and neuronal death by excessive stimulation of NMDA receptors, the incomplete blockade of the NMDA receptors minimizes the intensity of the abstinence syndrome and provides the downregulation of the receptors. In the present study, tizanidine (TIZ), which inhibits the release of endogenous excitatory aminoacids by the agonistic activity on .alpha.2-adrenoreceptors, was combined with DM to obtain further benefits. Forty-four male and three female heroin addicts were the subjects of the study. Their daily mean heroin intake was about 2.28 g street heroin. The main duration of heroin use was approximately 3.4 years. Two to three hours after abrupt withdrawal, the outpatients were given 15 mg DM every hour, 25 or 50mg chlorpromazine (CPZ) + 4mg TIZ every six hours and 10mg diazepam + 10 mg hyoscine N-butyl Br + 250 mg dipyrone every six hours three hours following CPZ. The addicts were controlled twice a day. Yawning, **rhinorrhea**, perspiration, piloerection, restlessness, insomnia, **emesis**, diarrhea, craving, rejection of smoking and pupils were observed and/or questioned. Two of the 47 outpatients took heroin on the first days. The others were heroin-free at least throughout the treatment period of eight days. A shorter-lasting abstinence syndrome with considerably less intense signs was observed. Craving, insomnia, **emesis**, diarrhea, restlessness, rejection of smoking appeared markedly attenuated. Since TIZ binds to the imidazoline receptor with approximately 20 times higher affinity than the .alpha.2-adrenoreceptors, TIZ may attenuate intensity of opiate abstinence syndrome via I]

imidazoline-receptors.

L9 ANSWER 11 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94304974 EMBASE
DOCUMENT NUMBER: 1994304974
TITLE: Preoperative assessment and preparation.
AUTHOR: Griffith K.E.
CORPORATE SOURCE: Anesthesiology/Pain Management Dept., Texas University SW Medical Center,Dallas, TX, United States
SOURCE: International Anesthesiology Clinics, (1994) 32/3 (17-36).
ISSN: 0020-5907 CODEN: IACLAV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 009 Surgery
024 Anesthesiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The practice of ambulatory surgery is rapidly expanding, not only the type of surgeries performed, but more 'at risk' patients are being allowed outpatient procedures. Warner and colleagues [56] recently published the results of a large prospective outcome survey of morbidity and mortality after ambulatory surgery. Of the 38,598 patients studied, 31 patients experienced a major morbidity (1:1455) and 4 died (2 myocardial infarctions and 2 motor vehicle accidents) (Table 7). There were no deaths secondary to medical complications within the first week after ambulatory surgery. Furthermore, the morbid events were equally distributed among the various ASA classification categories (Table 8). Given the overall low morbidity and mortality rates, it is likely that ambulatory surgery will continue to grow in the future. Improved preoperative assessment and preparation will further increase the number of acceptable candidates for ambulatory surgery. Having recognized the special needs of the surgical outpatient, anesthesiologists should modify their practice patterns to meet the psychological and pharmacological requirements of the outpatient undergoing an elective surgical procedure.

L9 ANSWER 12 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 93249923 EMBASE
DOCUMENT NUMBER: 1993249923
TITLE: Other agents: Phencyclidine, marijuana, hallucinogens, inhalants, and anticholinergics.
AUTHOR: Brust J.C.M.
CORPORATE SOURCE: Department of Neurology, Harlem Hospital Center, 506

Lenox Avenue,New York, NY 10037, United States
SOURCE: Neurologic Clinics, (1993) 11/3 (555-561).
ISSN: 0733-8619 CODEN: NECLEG
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Acute phencyclidine intoxication causes psychosis and a myriad of other symptoms and signs, some life-threatening. Anticholinergic poisoning is also a medical emergency, often requiring an intensive care unit. Marijuana and hallucinogens have rarely, if ever, resulted in direct overdose death, but intoxication can result in accidents or self-injury. Inhalants cause death from cardiac arrhythmia, suffocation, or accident. Each of these agents is associated with a variety of medical and neurologic complications, some of which are discussed at greater length elsewhere in this issue.

L9 ANSWER 13 OF 17 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1992-141427 [17] WPIDS
DOC. NO. CPI: C1992-065710
TITLE: **Intranasal** admin. of **scopolamine** - as anticholinergic agent, with higher bio-availability than oral admin. and without the induced amnesia of IV admin..
DERWENT CLASS: B02
INVENTOR(S): CINTRON, N M; PUTCHA, L
PATENT ASSIGNEE(S): (USAS) NAT AERO & SPACE ADMIN
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 7765615	A	19920310	(199217)*		12

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 7765615	A	US 1991-765615	19910925

PRIORITY APPLN. INFO: US 1991-765615 19910925
AN 1992-141427 [17] WPIDS
AB US 7765615 A UPAB: 19931006

Scopolamine is administered **intranasally**.

This can be in the form of aq. **nasal** drops, mist spray, aerosol mist, gel or ointment. The drug may be formulated in a buffered saline soln. A dose of 0.4mg is satisfactory and doses of up to at least 0.6 mg may be used. The soln. p1-1 is suitably 4 +/- 0.2.

USE/ADVANTAGE - **Scopolamine** is an anticholinergic agent and is used to treat **motion sickness**, by oral admin. or topical patch and as a pre-operative treatment, generally given i.v. to inhibit secretions during anesthesia and surgery. When administered orally **scopolamine** is broken down in the liver and its bioavailability is reduced by the present **intranasal** administration, provides high bioavailability and is also without the drawback of drug-induced amnesia by i.v. delivery. Also **intranasal** delivery, unlike i.v. is not invasive and compsn. for it are inexpensive to formulate in multiple dose quantities. (0/1)

0/1

L9 ANSWER 14 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 92071010 EMBASE
DOCUMENT NUMBER: 1992071010
TITLE: Analgesia for day surgery.
AUTHOR: Baker A.B.
CORPORATE SOURCE: Dept of Anaesth and Int Care, Otago University,Dunedin, New Zealand
SOURCE: Medical Journal of Australia, (1992) 156/4 (274-280). ISSN: 0025-729X CODEN: MJAUAJ
COUNTRY: Australia
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Objective: To review current and potential analgesic techniques in day surgery with particular regard to their pharmacology. Data sources: Recent articles on analgesia for surgery and day surgery were retrieved from Index Medicus for 1988-1990. Pharmacokinetic data were collated from recent textbooks and articles. Data synthesis: The reviewed information is integrated with a pharmacological approach and personal experience with the use of postoperative analgesia. Conclusions: Combination analgesia therapy is the best approach for postoperative analgesia for day surgery. The usefulness of preoperative blockade of the pain sensation which limits activation of the central pain pathway and decreases analgesic requirements, is also emphasised. Examples of measures for

relief of mild, moderate and severe pain are given.

L9 ANSWER 15 OF 17 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88111046 EMBASE
DOCUMENT NUMBER: 1988111046
TITLE: Hormonal status and fluid electrolyte metabolism in **motion sickness**.
AUTHOR: Grigoriev A.I.; Nichiporuk I.A.; Yasnetsov V.V.; Shashkov V.S.
CORPORATE SOURCE: Institute of Biomedical Problems, Ministry of Health, 123007 Moscow, Russia
SOURCE: Aviation Space and Environmental Medicine, (1988) 59/4 (301-305).
ISSN: 0095-6562 CODEN: ASEMCG
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
002 Physiology
003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
035 Occupational Health and Industrial Medicine
030 Pharmacology
LANGUAGE: English

L9 ANSWER 16 OF 17 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 88177330 MEDLINE
DOCUMENT NUMBER: 88177330 PubMed ID: 3258431
TITLE: [Disoprivan (Propofol) sedation during regional anesthesia. A pilot study].
Disoprivan (Propofol) zur Sedierung wahrend der Regionalanaesthesie. Eine Pilotstudie.
AUTHOR: Dobler K; Dombrowski E; Nolte H
CORPORATE SOURCE: Institut fur Anaesthesiologie, Klinikum Minden, Minden/Westfalen.
SOURCE: REGIONAL ANAESTHESIE, (1988 Jan) 11 (1) 21-5.
Journal code: RCA; 8309693. ISSN: 0171-1946.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198805
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880503
AB In a preliminary pilot study, the effect of disoprivan for sedation during regional anesthesia was investigated. In 15 patients (ASA I or II), lumbar epidural anesthesia with bupivacaine 0.75% was

performed at L 3/4. For premedication morphine or pethidine combined with **scopolamine** was given. After injection of the local anesthetic, a 30-min period was allowed for establishing the physiological side effects of epidural blockade, to present any further changes in circulatory and/or cardiac function. Disoprivan (1 mg/kg body weight) was injected i.v. followed by continuous disoprivan infusion. Three groups of 5 patients each were given 1, 1.5, or 2 mg/kg per hour disoprivan. Changes in heart rate, blood pressure, and respiratory rate were studied. Recovery time and personal assessment of sleep were registered. Side-effects of clinical relevance from the cardiovascular and pulmonary systems were also registered. A dose-dependent upper airway obstruction that could easily be managed by an oral or **nasal** airway was seen in 9 of 15 patients. Eight patients had postoperative **nausea** or **vomiting**; 9 complained of pain during the bolus injection that they could not remember postoperatively. All patients described their sleep as pleasant. Recovery time from sleep was between 1 and 12 min. All changes from normal values increased in percentage with increasing disoprivan dosage. Disoprivan (1 or 1.5 mg/kg per hour) seems to be excellent for sedation during regional anesthesia and is perhaps even superior to other available drugs.

L9 ANSWER 17 OF 17 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1983-17380K [07] WPIDS
DOC. NO. CPI: C1983-016942
TITLE: Quick protection of subject against **motion sickness** - by application of spray contg. **scopolamine** into **nasal** passages.
DERWENT CLASS: B02
INVENTOR(S): KEITH, A D
PATENT ASSIGNEE(S): (KEYP) KEY PHARM INC
COUNTRY COUNT: 11
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8300286	A	19830203	(198307)*	EN	9
RW: AT BE CH DE FR GB LU NL SE					
W: JP					
EP 83373	A	19830713	(198329)	EN	
R: AT BE CH DE FR GB LI LU NL SE					
JP 58501129	W	19830714	(198334)		

PRIORITY APPLN. INFO: US 1981-283447 19810715
AN 1983-17380K [07] WPIDS

AB WO 8300286 A UPAB: 19930925
Person subject to a sudden turbulent motion is given protection against **motion sickness** by application of a spray contg. **scopolamine** (I) into the **nasal** passages, the protection starting when (I) enters the bloodstream.
The treatment confers quick relief against **motion sickness** compared with the usual oral or transdermal admin. of (I). The spray application is esp. valuable for people on an aircraft when sudden turbulence may be encountered, or on a crowded boat or ship.

FILE 'CAPLUS' ENTERED AT 10:30:30 ON 07 MAY 2001
L10 922 SEA FILE=CAPLUS ABB=ON PLU=ON HYOSCINE
L11 42 SEA FILE=CAPLUS ABB=ON PLU=ON L10 AND (NAUSEA? OR VOMIT? OR (MOTION OR AIR OR CAR OR SEA)(W)SICKNESS OR AIRSICKNESS OR CARSICKNESS OR SEASICKNESS OR EMESIS)
L12 0 SEA FILE=CAPLUS ABB=ON PLU=ON L11 AND (NASAL? OR NOSE OR RHINO? OR INTRANASAL? OR NOSTRIL)

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 10:35:09 ON 07 MAY 2001)
L13 8 S L12
L14 4 S L13 NOT L8
L15 2 DUP REM L14 (2 DUPLICATES REMOVED)

L15 ANSWER 1 OF 2 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 97:163592 SCISEARCH
THE GENUINE ARTICLE: WH825
TITLE: Anticholinergics improve fibreoptic intubating conditions during general anaesthesia
AUTHOR: Brookman C A (Reprint); Teh H P; Morrison L M
CORPORATE SOURCE: ROYAL INFIRM, DEPT ANAESTHET, 1 LAURISTON PL, EDINBURGH EH3 9YW, MIDLOTHIAN, SCOTLAND (Reprint); ST JOHNS HOSP, DEPT ANAESTHET, LIVINGSTON EH54 6PP, SCOTLAND
COUNTRY OF AUTHOR: SCOTLAND
SOURCE: CANADIAN JOURNAL OF ANAESTHESIA-JOURNAL CANADIEN D ANESTHESIE, (FEB 1997) Vol. 44, No. 2, pp. 165-167. Publisher: CANADIAN ANAESTHETISTS SOC INC, 1 EGLINTON AVE EAST, SUITE 208, TORONTO ON M4P 3A1, CANADA.
ISSN: 0832-610X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 10
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Purpose: To determine if anticholinergic agents improve

fibreoptic intubating conditions and to compare the efficacy and side effects of glycopyrrolate and **hyoscine**.

Methods: Eighty ASA I adults undergoing elective; wisdom tooth extraction were randomly allocated to receive 0.4 mg **hyoscine** hydrobromide po, 0.4 mg **hyoscine** hydrobromide im, 0.4 mg glycopyrrolate im or no anticholinergic, one hour pre-operatively. All underwent **nasal** fibreoptic intubation under general anaesthesia, The time taken to pass the fibreoptic scope was noted and visual analogue scores (VAS) were recorded for clarity of visual field and post-operative sore throat, dry mouth and **nausea**.

Results: The time to intubation was not different among the four groups (Kruschai-Wallis P = 0.07). The clarity oi visual field was improved in all three anticholinergic groups (Kruschal-Wallis P = 0.006), but there was no difference among the three groups (median VAS control 6.4, glycopyrrolate 8.0, oral **hyoscine** 7.9, im **hyoscine** 7.7). There was no difference in post-operative side effects among any of the groups at both 30 min and four hours.

Conclusion: The addition of an anticholinergic produced better visual conditions for intubation but had no effect on the incidence of post-operative sore throat, dry mouth and **nausea**.

L15 ANSWER 2 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95227448 MEDLINE
DOCUMENT NUMBER: 95227448 PubMed ID: 7711985
TITLE: The combination of tizanidine markedly improves the treatment with dextromethorphan of heroin addicted outpatients.
AUTHOR: Koyuncuoglu H
CORPORATE SOURCE: Department of Pharmacology and Clinical Pharmacology, Istanbul Medical Faculty, Capa-Istanbul, Turkey.
SOURCE: INTERNATIONAL JOURNAL OF CLINICAL PHARMACOLOGY AND THERAPEUTICS, (1995 Jan) 33 (1) 13-9.
Journal code: B0D; 9423309. ISSN: 0946-1965.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950524
Last Updated on STN: 19970203
Entered Medline: 19950518

AB According to the hypothesis implying that the main mechanism underlying opiate addiction is the blockade by opiates of NMDA receptor functions and subsequent upregulation and supersensitivity of the receptors, noncompetitive NMDA receptor blocker dextromethorphan (DM) has been successfully used in the heroin addict treatment. As the stimulation of NMDA receptors modulates the

release of neurotransmitters and hormones such as NE, D, ACh, GH, LH, LSH, ACTH etc., all of which have been found responsible for the manifestation of abstinence syndrome signs including craving and neuronal death by excessive stimulation of NMDA receptors, the incomplete blockade of the NMDA receptors minimizes the intensity of the abstinence syndrome and provides the downregulation of the receptors. In the present study, tizanidine (TIZ), which inhibits the release of endogenous excitatory aminoacids by the agonistic activity on alpha 2-adrenoreceptors, was combined with DM to obtain further benefits. Forty-four male and three female heroin addicts were the subjects of the study. Their daily mean heroin intake was about 2.28 g street heroin. The main duration of heroin use was approximately 3.4 years. Two to three hours after abrupt withdrawal, the outpatients were given 15 mg DM every hour, 25 or 50 mg chlorpromazine (CPZ) + 4 mg TIZ every six hours and 10 mg diazepam + 10 mg **hyoscine** N-butyl Br + 250 mg dipyrone every six hours three hours following CPZ. The addicts were controlled twice a day. Yawning, **rhinorrhea**, perspiration, piloerection, restlessness, insomnia, **emesis**, diarrhea, craving, rejection of smoking and pupils were observed and/or questioned. Two of the 47 outpatients took heroin on the first days. (ABSTRACT TRUNCATED AT 250 WORDS)

FILE 'MEDLINE' ENTERED AT 10:36:12 ON 07 MAY 2001

FILE LAST UPDATED: 2 MAY 2001 (20010502/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

L16	4457	SEA	FILE=MEDLINE ABB=ON	PLU=ON	SCOPOLAMINE/CT
L17	1269	SEA	FILE=MEDLINE ABB=ON	PLU=ON	"MOTION SICKNESS"/CT
L18	11370	SEA	FILE=MEDLINE ABB=ON	PLU=ON	VOMITING/CT

Searcher : Shears 308-4994

L19 7432 SEA FILE=MEDLINE ABB=ON PLU=ON NAUSEA/CT
L20 246 SEA FILE=MEDLINE ABB=ON PLU=ON L16 AND (L17 OR L18 OR L19)
L21 4762 SEA FILE=MEDLINE ABB=ON PLU=ON "ADMINISTRATION, INTRANASAL"/CT
L22 0 SEA FILE=MEDLINE ABB=ON PLU=ON L20 AND L21

L16 4457 SEA FILE=MEDLINE ABB=ON PLU=ON SCOPOLAMINE/CT
L21 4762 SEA FILE=MEDLINE ABB=ON PLU=ON "ADMINISTRATION, INTRANASAL"/CT
L23 2 SEA FILE=MEDLINE ABB=ON PLU=ON L16 AND L21

L23 ANSWER 1 OF 2 MEDLINE
AN 97016661 MEDLINE
TI Bioavailability of intranasal scopolamine in normal subjects.
AU Putcha L; Tietze K J; Bourne D W; Parise C M; Hunter R P; Cintron N M
SO JOURNAL OF PHARMACEUTICAL SCIENCES, (1996 Aug) 85 (8) 899-902. Journal code: JO7; 2985195R. ISSN: 0022-3549.
AB The bioavailability of scopolamine in three dosage forms was compared in 12 healthy nonsmoking male volunteers. Subjects received 0.4-mg doses of scopolamine bromide in intravenous (i.v.), intranasal (i.n.), or oral (p.o.) dosage forms on three occasions, with at least 2 weeks separating the doses. Scopolamine concentrations in plasma were determined with a combined reverse-phase liquid chromatographic-radioreceptor binding assay. Saliva volume and flow rate and percent suppression of control flow rate were determined from each sample. Absorption after i.n. and po scopolamine administration was rapid; plasma concentrations [1680 (i.n.) and 164 pg/mL (p.o.)] peaked within 1 h of dosing [0.37 (i.n.) and 0.78 h (p.o.)], respectively. i.n. and i.v. scopolamine suppressed salivary flow rate to similar extents (95% and 99.7%), respectively. Times to reach maximum effect were 1.05 and 0.27 h after i.n. and i.v. dosage, respectively. Absolute intranasal bioavailability, calculated from the area under the drug concentration vs time curve, was found to be significantly greater than that of p.o. scopolamine (83% vs 3.7%, $p < 0.05$). The i.n. route may provide a noninvasive, reliable, fast, and effective route for administering scopolamine.

FILE 'CAPLUS' ENTERED AT 10:39:44 ON 07 MAY 2001
L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SCOPOLAMINE/CN
L2 1 SEA FILE=REGISTRY ABB=ON PLU=ON "SCOPOLAMINE BROMIDE"/CN
L3 2 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2
L4 6773 SEA FILE=CAPLUS ABB=ON PLU=ON L3 OR SCOPOLAMINE OR SCOPOL AMINE

L10 922 SEA FILE=CAPLUS ABB=ON PLU=ON HYOSCINE
L26 28 SEA FILE=CAPLUS ABB=ON PLU=ON (L4 OR L10)(L)(NASAL? OR NOSE OR RHINO? OR INTRANASAL? OR NOSTRIL)

L27 23 S L26 NOT L7

L35 12 S L27 AND ADMIN?

L35 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:895391 CAPLUS
TITLE: A descriptive study of an epidemic of poisoning caused by heroin adulterated with scopolamine
AUTHOR(S): Hamilton, Richard J.; Perrone, Jeanmarie; Hoffman, Robert; Henretig, Fred M.; Karkevandian, Eb H.; Marcus, Steven; Shih, Richard D.; Blok, Barbara; Nordenholz, Karen
CORPORATE SOURCE: New York City Poison Center, New York University School of Medicine, New York, NY, USA
SOURCE: J. Toxicol., Clin. Toxicol. (2000), 38(6), 597-608
CODEN: JTCTDW; ISSN: 0731-3810
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adulterants, contaminants, and diluents are all examples of additives to street drugs. Some of these additives may be pharmacol. active; however, it is unusual for them to cause toxic side effects. In the spring of 1995, a new form of heroin appeared in New York City, spreading to other East Coast cities, that was adulterated with **scopolamine**. It caused severe anticholinergic toxicity in heroin users with patients often presenting to emergency departments in great nos. This is a report of the demographics and clin. characteristics of the epidemic. A combination of prospective and retrospective data collection from the New York City, New Jersey, Delaware Valley, and Maryland Poison Centers. The primary measurements were age, sex, route of drug use, vital signs, signs and symptoms, disposition, and treatment. Of the 370 cases reported to the participating poison centers, 129 were excluded from the final anal. because of insufficient data. Of the patients who used this product, 55% presented with signs and symptoms of heroin toxicity. But then became severely agitated with anticholinergic symptoms when naloxone was used to reverse respiratory depression. **Nasal** insufflation was the route of **administration** in 34% of the cases. Seizures were rare (3%). Ninety percent required admission, and half were admited to a crit. care unit. Adulteration of street drugs can lead to toxic epidemics. Poison centers are essential for identification of these trends and are the primary source of information on diagnosis and

treatment.
REFERENCE COUNT: 30
REFERENCE(S):
(1) Barnfield, C; Foren Sci Int 1988, V39, P107 CAPLUS
(3) Bogan, J; J Sci Soc 1966, V6, P166 CAPLUS
(7) Chiarotti, M; Foren Sci Int 1983, V21, P245 CAPLUS
(8) Chiarotti, M; Foren Sci Int 1991, V50, P47 CAPLUS
(18) Kaa, E; Foren Sci Int 1986, V31, P195 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:865098 CAPLUS
DOCUMENT NUMBER: 134:21487
TITLE: Nasal pharmaceutical compositions for water-insoluble and/or difficulty water-soluble drugs
INVENTOR(S): Kloecker, Norbert
PATENT ASSIGNEE(S): Hexal A.-G., Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19925290	A1	20001207	DE 1999-19925290	19990602
WO 2000074651	A1	20001214	WO 2000-EP4799	20000526

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 1999-19925290 A 19990602
DE 1999-19936543 A 19990803

AB A pharmaceutical compn. for nasal **administration** consists of at least a water-insol. or difficulty water-sol. drug which is dissolved in neutral oil. This pharmaceutical compn. can be **administered**, without the addn. of preservatives, by means of devices, which produce an exactly defined dose on the nose mucous

membrane. Thus, beclomethasone dipropionate was dissolved in Miglyol-840 and the soln. was filtered and filled into a pump spray. The drug concn. was 100 .mu.g in 140 .mu.L spray.

IT **51-34-3, Scopolamine**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nasal** pharmaceutical compns. for water-insol. drugs)

L35 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:793411 CAPLUS
DOCUMENT NUMBER: 132:317873
TITLE: Intravenous Scopolamine Is Potently Self-**Administered** in Drug-Naive Mice
AUTHOR(S): Rasmussen, T.; Fink-Jensen, A.
CORPORATE SOURCE: Health Care Discovery, Novo Nordisk A/S, Novo Nordisk Park, Den.
SOURCE: Neuropsychopharmacology (1999), Volume Date 2000, 22(1), 97-99
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Scopolamine** self-**administration** was investigated in an acute model using drug-naive mice. The mice could self-**administer** i.v. infusions contingent on **nose** poking and were tested in pairs using a contingent and a yoked control mouse. Upon **nose** poking of the contingent mouse, both mice received an i.v. infusion of either saline or **scopolamine** (fixed ratio 1). An inverted U-shaped unit dose-response curve was seen with the contingent mice. The unit dose at which **nose** poking of the contingent mice peaked (mean 375 per 30 min) was 0.1 mg/kg/infusion. **Nose** poking of yoked control mice also increased dose dependently, but it was significantly lower than that of the contingent mice. The apparent **scopolamine**-induced dose-dependent hyperactivity was, however, unlikely in itself to form the entire basis for the increase in **nose** poking of the contingent mice. The results demonstrate that **scopolamine** has acute and reinforcing properties in drug naive mice.

REFERENCE COUNT: 18
REFERENCE(S):
(1) Aigner, T; Pharmacol Biochem Behav 1979, V10, P105 CAPLUS
(3) Bymaster, F; Eur J Pharmacol 1998, V356, P109 CAPLUS
(5) Fink-Jensen, A; NeuroReport 1998, V9, P3481 CAPLUS
(7) Glick, S; Life Sci 1982, V31, P909 CAPLUS
(11) Kuzmin, A; Pharmacol Biochem Behav 1992, V41, P497 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:413732 CAPLUS
DOCUMENT NUMBER: 129:184141
TITLE: An automated learning and memory model in mice: pharmacological and behavioral evaluation of an auto-shaped response
AUTHOR(S): Vanover, K. E.; Barrett, J. E.
CORPORATE SOURCE: Medical Research Division, Lederle Laboratories, Central Nervous System Research Department, American Cyanamid Co., Pearl River, NY, USA
SOURCE: Behav. Pharmacol. (1998), 9(3), 273-283
CODEN: BPHAEL; ISSN: 0955-8810
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of the present expts. was to develop and validate pharmacol. an automated, relatively rapid, and reproducible behavioral model of learning and memory using an auto-shaping procedure in mice. **Nose**-poke responses into a recessed area were differentiated by response-dependent reinforcement during two identical consecutive daily sessions. Performance during the first session was considered to be a measure of acquisition and that during the second session a measure of retention. Sensitivity to procedural manipulation, as well as an index of learning under these conditions, was demonstrated, for example, by a decrease in response rate when **nose**-poke responses did not produce a reinforcer. The sensitivity of the paradigm to pharmacol. intervention was examd. after drug **administration** before the first session. **Scopolamine** (0.1-10.0 mg/kg) had no effect on acquisition but caused a significant dose-related impairment of retention. Dizocilpine (0.01-1.0 mg/kg) impaired both acquisition and retention performance. 8-Hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT; 0.1-1.0 mg/kg) disrupted behavior in general, but failed to have a selective effect on acquisition or retention. Linopirdine (0.1-1.0 mg/kg) showed only a weak enhancement of acquisition, whereas 4-aminopyridine (4-AP; 0.1-1.0 mg/kg) significantly facilitated acquisition. This paradigm offers the potential for a rapid, objective, and reliable indication of whether a drug will affect the acquisition or retention of a pos. reinforced response in mice and could be a useful supplement to existing procedures.

L35 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:594624 CAPLUS
DOCUMENT NUMBER: 127:210389
TITLE: Powdery composition for nasal

administration

INVENTOR(S): Dohi, Masahiko; Nishibe, Yoshihisa; Makino, Yuji; Fujii, Takao

PATENT ASSIGNEE(S): Teijin Ltd., Japan; Dohi, Masahiko; Nishibe, Yoshihisa; Makino, Yuji; Fujii, Takao

SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731626	A1	19970904	WO 1997-JP541	19970226
W: AU, CA, CN, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 10059841	A2	19980303	JP 1996-261837	19961002
JP 09291025	A2	19971111	JP 1996-262899	19961003
CA 2247191	AA	19970904	CA 1997-2247191	19970226
AU 9722302	A1	19970916	AU 1997-22302	19970226
AU 722319	B2	20000727		
CN 1216464	A	19990512	CN 1997-193861	19970226
EP 943326	A1	19990922	EP 1997-905398	19970226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

JP 1996-39553	A	19960227
JP 1996-41079	A	19960228
JP 1996-154078	A	19960614
WO 1997-JP541	W	19970226

AB The inventions relate to a powdery compn. for nasal **administration** wherein: (1) the compn. comprises (i) a medicament, (ii) a water-absorbent, gel-forming base such as hydroxypropylcellulose or hydroxypropylmethylcellulose, and (iii) a water-absorbent, sparingly water-sol. base such as cryst. cellulose or .alpha.-cellulose; (2) the amt. of the water-absorbent, gel-forming base is about 5 to 40 % by wt. of the sum of the amts. of the water-absorbent, gel-forming base and the water-absorbent, sparingly water-sol. base; and (3) the medicament is unevenly dispersed in the water-absorbent, sparingly water-sol. base rather than in the water-absorbent, gel-forming base. The compn. is advantageous in that an excellent absorption via the nasal cavity can be offered even in the case of a highly water-sol. medicament, a highly liposol. medicament, and a high-mol. wt. peptide or protein medicament and the max. blood level is much larger than that for the conventional compns. for nasal **administration**.

IT **51-34-3, Scopolamine**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(powdery compn. for **nasal administration**)

L35 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:417821 CAPLUS
DOCUMENT NUMBER: 125:67443
TITLE: Bioavailability of **Intranasal Scopolamine** in Normal Subjects
AUTHOR(S): Putcha, Lakshmi; Tietze, Karen J.; Bourne, David W. A.; Parise, Cecelia M.; Hunter, Robert P.; Cintron, Nitza M.
CORPORATE SOURCE: Johnson Space Center, NASA, Houston, TX, USA
SOURCE: J. Pharm. Sci. (1996), 85(8), 899-902
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bioavailability of **scopolamine** in 3 dosage forms was compared in 12 healthy nonsmoking male volunteers. Subjects received 0.4-mg doses of **scopolamine** bromide in i.v., **intranasal** (IN), or oral (PO) dosage forms on 3 occasions, with at least 2 wk sepg. the doses. Absorption after IN and PO **scopolamine administration** was rapid; plasma concns. [1680 (IN) and 164 pg/mL (PO)] peaked within 1 h of dosing [0.37 (IN) and 0.78 h (PO)], resp. IN and i.v. **scopolamine** suppressed salivary flow rate to similar extents (95% and 99.7%), resp. Times to reach max. effect were 1.05 and 0.27 h after IN and i.v. dosage, resp. Abs. **intranasal** bioavailability, calcd. from the area under the drug concn. vs time curve, was found to be significantly greater than that of PO **scopolamine** (83 vs 3.7%). The IN route may provide a noninvasive, reliable, fast, and effective route for **administering scopolamine**.
IT **51-34-3, Scopolamine**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability of **intranasal scopolamine** in humans)

L35 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:605128 CAPLUS
DOCUMENT NUMBER: 117:205128
TITLE: Scopolamine increases nonreinforced behavior in an intracranial self-stimulation discrimination paradigm
AUTHOR(S): Agars, Karen; Kokkinidis, Larry
CORPORATE SOURCE: Dep. Psychol., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SOURCE: Pharmacol., Biochem. Behav. (1992), 43(2),

657-60
CODEN: PBBHAU; ISSN: 0091-3057
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of several doses of systemic **scopolamine administration** on brain-stimulation reward from the A10 nucleus of the ventral tegmental area (VTA) were evaluated. The intracranial self-stimulation (ICSS) task involved a two-hole **nose**-poke procedure allowing for the assessment of both reinforced (correct) and nonreinforced (incorrect) performance levels as a function of varying current intensities. **Scopolamine** (0.75, 1.5, and 3.0 mg/kg) was found not to alter the rate-intensity functions derived from descending and ascending presentation of seven current levels. However, when nonreinforced behavior was considered significant increases in error responding were evident following **scopolamine** injection. These results are consistent with the known disinhibitory and perseverative properties of **scopolamine**, and indicate that the previously reported pos. actions of peripheral **administration** of anticholinergic drugs on ICSS likely involved a drug-induced rate-enhancement of reward-unrelated performance variables.

L35 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:171336 CAPLUS
DOCUMENT NUMBER: 114:171336
TITLE: Stabilized tropane alkaloid sprays
INVENTOR(S): Lettko, Herbert
PATENT ASSIGNEE(S): Aerochem Herbert Lettko G.m.b.H. und Co. K.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 3 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3926751	A1	19910214	DE 1989-3926751	19890812

AB Alc. soln. of tropane alkaloids are stabilized by the addn. of 1.5-1.7 mm microspheres made of mol. sieves, such as zeolite. The solns. are **administered** nasally, as aerosol sprays. The unit dose contains 1.65 mg atropine base.

IT **51-34-3, Scopolamine**
RL: PROC (Process)
(**nasal** formulation of, as stabilized aerosol spray)

L35 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:142640 CAPLUS
DOCUMENT NUMBER: 104:142640
TITLE: Motor effects of calcitonin **administered** intracerebroventricularly in the rat
AUTHOR(S): Twery, Michael J.; Kirkpatrick, Brian; Critcher, Elizabeth C.; Lewis, Mark H.; Mailman, Richard B.; Cooper, Cary W.
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Eur. J. Pharmacol. (1986), 121(2), 189-98
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In rats treated with salmon calcitonin (CT) [47931-85-1] **administered** intracerebroventricularly (i.c.v., 85 or 8.5 pmol), spasmodic body movements, hopping, and tail jerks, collectively termed dyskinesia, appeared within 1 h of **administration** and persisted for at least 24 h. In addn., spontaneous grooming, rearing, and locomotion occurred less often in CT-treated rats than in vehicle-injected animals, whereas the incidence of both sniffing and **nose** poking remained essentially unchanged. The CT failed to displace either [3H]dopamine or [3H]spiperone from striatal membranes, and the behavioral effects were not blocked by haloperidol or SCH 23390, suggesting that the peptide did not directly affect dopamine receptors. The dyskinesia was not blocked by **scopolamine**, atropine, muscimol, diazepam, or ketanserin. Apparently, a compd. with recognition characteristics similar to those of salmon CT may function as a neurotransmitter-modulator in the central nervous system.

L35 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1967:489342 CAPLUS
DOCUMENT NUMBER: 67:89342
TITLE: In vivo antiviral chemotherapy. II. Antiinfluenza action of compounds affecting mucous secretions
AUTHOR(S): Streightoff, Frank; Redman, Charles E.; DeLong, Donald C.
CORPORATE SOURCE: Eli Lilly and Co., Indianapolis, Indiana, USA
SOURCE: Antimicrob. Agents Chemother. (1961-70) (1966) 503-8
CODEN: AACHAX
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pilocarpine, a parasympathomimetic agent which stimulates the secretion of mucus, **administered** i.p. prior to aerosol infection of mice by PR-8A influenza virus, increased the severity

of the disease as measured by the survival index. Acetyl-.beta.-methylcholine iodide, another cholinergic compd., had a similar effect. The anticholinergic drugs, atropine sulfate and **scopolamine** hydrobromide, **administered** i.p. before infection, decreased the severity of the disease. Heteronium bromide, an inhibitor of gastric secretion, also reduced the severity of influenza in mice. N-Acetyl-L-cysteine, which has mucolytic activity and is used to liquefy sputum, when **administered intranasally** prior to aerosol infection by influenza virus, reduced the severity of the disease. Cysteine-HCl also had a similar protective effect when **administered intranasally**. Although mucus may play a protective role against influenza virus in mice, the changes in quantity and compn. of mucus induced by the drugs used in the present study did not verify this concept. The 2 cholinergic drugs which increased mucus secretion increased the severity of the disease; the 3 anticholinergic drugs which reduced mucous secretion decreased the severity of disease; the 2 mucolytic drugs which modified the mucus present decreased the severity of the disease. The findings suggest either that mucus does not play a protective role in the resistance of mice to influenza virus or that other effects of these drugs obscure the protective effect of mucus. 15 references.

L35 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1957:93596 CAPLUS
DOCUMENT NUMBER: 51:93596
ORIGINAL REFERENCE NO.: 51:16970e-g
TITLE: Selective activity of morphine on the "EEG arousal reaction" to painful stimuli
AUTHOR(S): Silvestrini, B.; Longo, V. G.
CORPORATE SOURCE: Ist. super. Sanita, Rome
SOURCE: Experientia (1956), 12, 436-7
DOCUMENT TYPE: Journal
LANGUAGE: English
AB After the **administration** of 5-10 mg./kg. morphine intravenously into unanesthetized noncurarized rabbits, a selective depression of the arousal reaction (desynchronization of the electroencephalogram) following painful stimuli can be noted; the arousal reaction to sensory stimulation, such as blowing on the **nose**, buzzer, and touching of the back, remains unaffected. Simultaneously there is an increase in the stimulation threshold of the anteromedial nuclei of the thalamus without a similar variation at the mesencephalic level. As the dose is increased to 10-25 mg./kg., the selective effect is less marked. A similar specificity is not displayed by the barbiturates and **scopolamine**.

L35 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1950:44539 CAPLUS
DOCUMENT NUMBER: 44:44539
ORIGINAL REFERENCE NO.: 44:8518f-i,8519a-c
TITLE: Pharmacological studies of the masseter muscle of the rat
AUTHOR(S): Hotovy, Rudolf; Erdniss, Helga
CORPORATE SOURCE: Univ., Heidelberg, Germany
SOURCE: Arch. exptl. Path. Pharmakol. (1950), 209, 204-34
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 43, 7070a for app. used. Asphyxiation with illuminating gas or by obstruction of the **nasal** passages produced a drop in the work capacity of the electrically stimulated masseter muscle. Emergency mechanisms (adrenaline) restored the muscle's power. N2O behaved similarly to illuminating gas, but the restoration of muscular ability often failed to appear. Na-, iso-Bu-, and AmNO2 as vasodilators had no direct influence on muscular performance. The methemoglobin formation which they caused resulted in loss of power which could only occasionally be relieved by thionine or methylene blue. After nitrite **administration**, prostigmine (I) and adrenaline had little or no effect. Caffeine, and to a lesser extent theophylline and theobromine, had a peripheral stimulatory effect on the muscle. Coramine alone had no effect in the intact animal, but the synergism between it and I was confirmed. Adrenaline about doubled muscular performance, while ephedrine and arterenol had less effect, and privine had none. Gynergen, hydergin, and dibenamine inhibited, and dihydroergotamine was weakly antagonistic to, the effect of I. Only I exceeded digitoxin and g- and k-strophanthin in their ability to improve muscle performance. Corhormone (ext. of embryonic heart) did not affect the muscle. Digitalis, K+, and Ba++ also improved the muscle's work output. I, eserine, and ([2?-] hydroxy-[5?-] phenylbenzyl)trimethylammonium dimethylcarbamate showed their usual effect on striated muscle. Doryl had a weak stimulatory effect, and choline had none. Iodomethylcodeine acted synergistically with I. Curare inhibited the normal and I-treated muscle without affecting its respiration. Subsequently **administered** I was fully active, and repeated doses of curare had a cumulative effect. **Scopolamine** had no effect on the I-treated muscle, while apoatropine was weakly antagonistic to I. Atropine and butylscopolamine showed a "lissive action." The effect of the latter was fleeting. Diparcol, harmine, parpanit, myanesin, bulbocapnine, papaverine, eupaverine, and neupaverine (slightly) also antagonized I. This action was manifested slowly and lasted long in the case of the first 2. **Administration** of I after these 2 or atropine had little or no effect. Except for a lack of central action, trasentin behaved similarly. Cocaine,